UTILIZATION AND PERCEPTIONS OF HEALTHCARE FROM A NATIONAL SURVEY OF FAMILIES WITH DUCHENNE MUSCULAR DYSTROPHY

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ABSTRACT

Duchenne muscular dystrophy (DMD) is a progressive neuromuscular disorder that creates significant healthcare needs and greatly impacts families. As interventions improving life quality and expectancy have become available and as care recommendations have been established, it has become increasingly important to understand what services families are utilizing and their perceptions of this care. This study describes data from the US National Initiative for Families with Duchenne (NIFD) questionnaire, which was designed in part to explore these aspects of families' experiences. Differences between sub-populations in the dataset and associations between survey variables were analyzed. NIFD data were compared to data from a more recent patient registry, DuchenneConnect (DC), which also assesses healthcare utilization in individuals with DMD.

Child's health status and medical care variables were examined from 191 NIFD surveys completed by family members of children with DMD. While many families were receiving multidisciplinary care, timing of first visits and the need for certain providers were shown as areas where families could use more education. Socioeconomic differences between NIFD sub-populations revealed possible explanations for differences in care. Factors associated with pain frequency and overall life satisfaction in individuals with DMD emphasize the need for multidisciplinary care and provide areas where healthcare providers can assist families.

Comparison of NIFD and DC data revealed a wider phenotypic spectrum in the latter group. DC registrants reported less problems with certain medical expenses and higher use of therapies. These differences point to the need to assess a large population to develop an accurate picture of DMD and hopefully indicate that awareness and access to important services and interventions has improved over time.

DMD is the most common fatal genetic disorder affecting children across all ethnic backgrounds. This high, pan-ethnic incidence as well the significant impact of the disease on individuals with DMD and their families make this a condition of public health concern. Understanding service utilization as well as families' perceptions of it will help in addressing potential gaps and barriers experienced in caring for individuals with DMD and will thus inform public health policies to help these families.

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PREFACE

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1.0 INTRODUCTION

Duchenne muscular dystrophy (DMD) is a neuromuscular disorder with X-linked inheritance. It is one of the most common genetic conditions with an incidence of about 1 in 3,300 to 5,300 male births. Mutations in the gene encoding the dystrophin protein lead to progressive loss of muscle strength in major body systems, ultimately causing loss of the ability to walk and perform daily activities and eventually death.

The impact of this debilitating condition on those affected by it and their families is significant. While a cure has not yet been identified, the development of new treatments and interventions over time has greatly enhanced the quality of life and life expectancy of individuals with DMD. These developments have come about with the cooperation of multiple groups including researchers, physicians and parents of children with DMD. The Cooperative International Neuromuscular Research Group (CINRG) has been one of the key players in DMD clinical research with its network of US and international study sites.

As the natural history of DMD and the effects of newer interventions have been studied, a move towards establishing care guidelines has developed over the last decade. The sum of these efforts has resulted in DMD care recommendations in 2010. These documents outline key areas of complex multidisciplinary care, with the aim of standardizing and diminishing disparities in the care of those with DMD. As these guidelines have evolved it has been less clear what kind of care families are actually receiving as well as their perceptions of this care and its impacts. Thus,

several efforts have been launched to better understand these aspects of families' experiences. The National Initiative for Families with Duchenne (NIFD) survey was developed in partnership with the Center for Disease Control and Prevention (CDC) to assess the experiences and needs for US families with DMD. Data were obtained between 2006 and 2009. This present study analyzes data from the NIFD survey to explore healthcare utilization as well as families' perceptions of it and how it may impact families. The relationships between demographic and other variables were analyzed to identify differences in access and use of various services and interventions. Data from DuchenneConnect (DC), a US patient registry with data from 2007 to 2013, were compared to NIFD data to assess similarities and differences with another DMD patient population.

Understanding what services families are utilizing and identifying potential barriers to them is important in establishing a global standard of care for those with DMD. This knowledge will complement current efforts to develop DMD centers of excellence and initiatives to ensure the DMD care recommendations are actively integrated into the care of all individuals with DMD.

2.0 HYPOTHESIS AND SPECIFIC AIMS

2.1 HYPOTHESIS

As there is a move for standardization of care for DMD, families may not be receiving care consistent with recommendations due to differences in socioeconomic factors, perceived importance of care and availability of services.

2.2 SPECIFIC AIMS

Aim 1: To characterize demographic, health status, healthcare utilization and perceptions of care data from the NIFD survey.

Aim 2: To compare demographic and healthcare differences between NIFD sub-populations and explore associations between survey variables including those assessing impact and care received.

Aim 3: To compare NIFD data to data from DuchenneConnect, a web-based patient survey, to assess similarities and differences in healthcare utilization between the two populations.

3.0 BACKGROUND AND SIGNIFICANCE

3.1 DUCHENNE MUSCULAR DYSTROPHY

DMD is a progressive, neuromuscular disease predominantly affecting males with estimates of incidence between 1 in 3,300 to 1 in 5,300 of male live births (Engel and Banker 1986; Emery 1991; Bradley and Parsons 1998; Dooley et al. 2010). A population-based study from four US states estimated the prevalence of Duchenne/Becker muscular dystrophy (DBMD) to be 1.3 to 1.8 per 10,000 males age 5 to 24 years (Romitti et al. 2009). DMD is the most common fatal genetic condition in children (Hinton et al. 2001).

DMD is an X-linked condition associated with deletions, point mutations, and duplications in the dystrophin (*DMD*) gene. It is estimated that two thirds of cases inherit a dystrophin lesion from their mother while the remaining third possess a spontaneous mutation, owing to a high mutation rate in the *DMD* gene (Koenig et al. 1987; Bradley and Parsons 1998; Webb 2005). The dystrophin protein encoded by *DMD* serves as a stabilizing force within muscle structure (Gorospe and Hoffman 1992; Matsumura et al. 1993). Without functional dystrophin protein, the process of muscle degradation and regeneration is impaired leading to muscle wasting and replacement of muscle tissues with fat and connective tissue.

While one of the first signs of DMD, elevated creatine kinase levels, can be detected in the newborn period, physical manifestations of the disease are not usually recognized until the first to third year of life with diagnosis typically occurring by four to five years of age (Appleton and Nicolaides 1995; Bushby et al. 1999; Zalaudek et al. 1999; Parsons et al. 2004; Ciafaloni et al. 2009). These initial physical symptoms include developmental delays (locomotor, speech and cognitive in some) followed by abnormal gait, enlarged calves, toe-walking, frequent falls and clumsiness, muscle weakness and difficulty running, jumping, and climbing stairs (Firth et al. 1983; Bushby et al. 1999; Parsons et al. 2004; Ciafaloni et al. 2009). A range of learning and behavioral disorders (e.g. attention-deficit hyperactivity disorder and autism) has been consistently observed in some, though not all, boys with DMD (Hinton et al. 2001; Cyrulnik et al. 2007; Hendriksen and Vles 2008).

The progressive nature of the disease results in a gradual loss of ambulation with dependence on walking aids followed by full-time use of wheelchairs, typically in the early to mid-teens (McDonald et al. 1995; Biggar et al. 2006). Muscle contractures and scoliosis develop, further limiting abilities (Brooke et al. 1983; McDonald et al. 1995). As muscles continue to decline, cardiac and respiratory issues can ensue (Finder et al. 2004; English and Gibbs 2006; Vita et al. 2009) and usually become the cause of death in the 20s or 30s (Eagle et al. 2002; Brown Jr. et al. 2008). This presentation represents a common depiction of the natural history of DMD. Newer interventions and treatments discussed below, however, have shifted the progression of disease, development of scoliosis and life expectancy.

The progression of DMD has been generally classified into five stages: 1) pre-symptomatic, 2) early ambulatory, 3) late ambulatory, 4) early non-ambulatory and 5) late non-ambulatory. Though this disease course is usually predictable, variation in the onset of symptoms

and overall phenotype among patients has been described (Brooke et al. 1983; Brooke et al. 1989; Desguerre et al. 2009). Additionally, while not the topic of this work, Becker muscular dystrophy (BMD) is a less common, allelic condition with similar albeit later onset of symptoms than DMD. As better recognition of and enhanced treatments for DMD become available the hope is that this clinical course will continue to improve, as it has been over the last several decades.

3.2 CARE RECOMMENDATIONS FOR MANAGEMENT OF DMD

In the absence of a cure, management for patients with DMD has focused on slowing down the disease progression while maintaining quality of life. Given the multi-system effects DMD has on the body, management of the condition is complex, typically involving multiple specialists. The model is for individuals to access this care through a multidisciplinary clinic. Increasing activism on the part of parents along with advances in knowledge and technology have generated a shift from non-interventional to more supportive and aggressive intervention (Finder et al. 2004; Webb 2005).

Consensus recommendations for single-system aspects of DMD care have been developed, for example in respiratory (Finder et al. 2004) and cardiovascular management (AAP 2005) and glucocorticoid use (Moxley et al. 2005). More recently Bushby et al issued comprehensive care recommendations for DMD in 2010 (hereafter, DMD care recommendations) through Centers for Disease Control and Prevention (CDC), European Union TREAT-NMD and patient advocacy groups and collaboration of over 80 experts (Bushby et al. 2010a; Bushby et al. 2010b). The DMD care recommendations were published in the Lancet

journal in two parts. Part 1 details diagnosis, pharmacological and psychosocial management and Part 2 details implementation of multidisciplinary care. The documents lay out recommendations for multi-system care (Figure 1) throughout five stages of DMD's course based on previous studies and ratings by expert opinion. The DMD care recommendations cover diagnosis, neuromuscular, rehabilitation, orthopedic, pulmonary, cardiac, gastrointestinal and psychosocial management. They emphasize the multi-disciplinary aspect essential to care of DMD, stating "no one aspect of the care of this disease can be taken in isolation" (Bushby et al. 2010b).

Prior to the development of these recommendations, early treatment approaches were focused on developing medications to slow the progression of DMD. Glucocorticoids have become a standard of care for DMD through multiple studies and clinical trials over several decades showing delay of declines in muscle strength and function (Drachman et al. 1974; DeSilva et al. 1987; Mendell et al. 1989; Fenichel et al. 1991; Griggs et al. 1993; Balaban et al. 2005; Biggar et al. 2006; Escolar et al. 2011). Benefits of treatment are observed as early as 3 months after initiation. The two main types of glucocorticoids are prednisone and deflazacort, recommended at doses of 0.75mg/kg per day and 0.9 mg/kg per day, respectively, and initiated when boys have reached a plateau (when motor skills are neither progressing nor declining) (Bushby et al. 2010a). The effect of the treatment on muscles in turn delays loss of ambulation by 2 or 5 years and development of scoliosis as well as stabilizes lung and heart function (Balaban et al. 2005; Biggar et al. 2006; Manzur et al. 2008; Moxley et al. 2010). Because of the latter benefits, continuation of glucocorticoids after ambulation loss is frequently practiced (Bushby et al. 2010a). Reduction in strength loss and preservation of functional capacities and lung function were recently shown to be preserved with chronic use of glucocorticoids (Henricson et al. 2013). Treatment side effects can be significant and include weight gain,

cataracts, behavioral changes, cushingoid facies, gastrointestinal complications and bone demineralization (Fenichel et al. 1991; Balaban et al. 2005; Biggar et al. 2005). A completed trial by CINRG (Escolar et al. 2011) and a continuing trial by the National Institutes of Health (NIH) (Griggs 2013) are aimed at determining ways to reduce side effects via different regimens (e.g. daily versus weekend) and assessing any differences in benefit between prednisone and deflazacort.

Other key interventions in DMD include physical therapy and assistive devices (splints, orthotics, standing devices) to maintain muscle flexibility and elongation and to prevent contractures (Brooke et al. 1989; McDonald et al. 1995; Bakker et al. 2000; Case 2006). Night splints, also called ankle-foot orthotics, are worn at night to prevent development and/or progression of contractures. After ambulation is lost, manual and power wheelchairs help individuals to maintain independence (Sussman 2002; Webb 2005). Spinal fusion may be indicated for scoliosis though the need for this surgery has been reduced as glucocorticoid use has become standard of care (Biggar et al. 2006; Moxley et al. 2010). Surgical interventions for contractures may also be indicated (Rideau et al. 1995; Sussman 2002).

Routine monitoring and ventilatory interventions, including cough assist, non-invasive nighttime ventilation and eventually daytime non-invasive or invasive ventilation address declining respiratory function (Eagle et al. 2002; Jeppesen et al. 2003; Finder et al. 2004). Cough assist devices aid in clearing the airway to prevent infection and collapse of the lungs. In-exsufflator devices, for example the Emerson Cough Assist device, mechanically simulate a cough for users. The DMD care recommendations strongly supports use of this type of device. Devices or approaches to move mucus, typically used in conjunction with cough assist devices, include intrapulmonary percussive ventilation (IPV), chest percussion, percussive nebulizer, and

pulmonary vests. Non-invasive ventilation devices, such as nasal intermittent positive pressure ventilation (NIPPV) with bi-level positive airway pressure (Bi-PAP) are recommended for DMD (Finder et al. 2004). Other non-invasive therapies such as continuous positive airway pressure (CPAP) and negative pressure ventilators are of limited use or should be used in a cautious manner. Tracheotomy is an example of invasive ventilation that should be considered if non-invasive techniques are not possible or feasible along with consideration of patient and family preference.

Cardiac care involves monitoring of function and treatment of complications (cardiomyopathy, arrhythmia) with standard cardiac medications including angiotensin-converting enzyme (ACE) inhibitors as well as beta-blockers and anti-diuretics (AAP 2005; English and Gibbs 2006). Psychosocial support for both the individual with DMD and his family is also indicated to address behavioral and emotional difficulties that arise through the course of living with DMD (Green and Murton 1996; Nereo et al. 2003; Abi Daoud et al. 2004).

Increased survival over time has been attributed to a number of factors including improved organization and delivery of care, use of flu immunizations and antibiotics, physical therapy, ventilatory support, scoliosis surgery and glucocorticoids (Eagle et al. 2002; Jeppesen et al. 2003; Bourke 2006; Kenneson et al. 2010). As care and interventions have improved so has lifespan, requiring more attention to be paid to previously less common complications, including those involving the heart and gastrointestinal tract (Baxter 2006; Manzur and Muntoni 2009). In addition, as more boys with DMD enter adulthood, attention has shifted toward improving the transition to adult care and including higher education and vocation training in long term plans (CDC 2009; Manzur and Muntoni 2009; Romitti et al. 2009). Increased awareness of palliative and end-of-life care for these families has been discussed (Finder et al. 2004; Madsen 2009;

Bushby et al. 2010a; Cohn 2010; Arias et al. 2011). The family is a key component in the care and support of individuals with DMD (Bostrom et al. 2006). Thus, recognition of the needs of the family as a unit is also important.

With the establishment of the DMD care recommendations and increased collaboration across interested stakeholders, current efforts are focused towards implementation of the care recommendations and improved access to care across multi-disciplinary sites. Through the collaboration of multiple non-profit organizations, family-friendly guides of the DMD care recommendations have been created in over 25 languages and are available for download from the Internet (http://www.treat-nmd.eu/care/dmd/family-guide/). Patient registries and initiatives, discussed further below, have also been developed to assess levels of care received, enhance family's knowledge and choices in DMD care, promote adoption of DMD care recommendations at clinics and establish centers of excellence in DMD care.

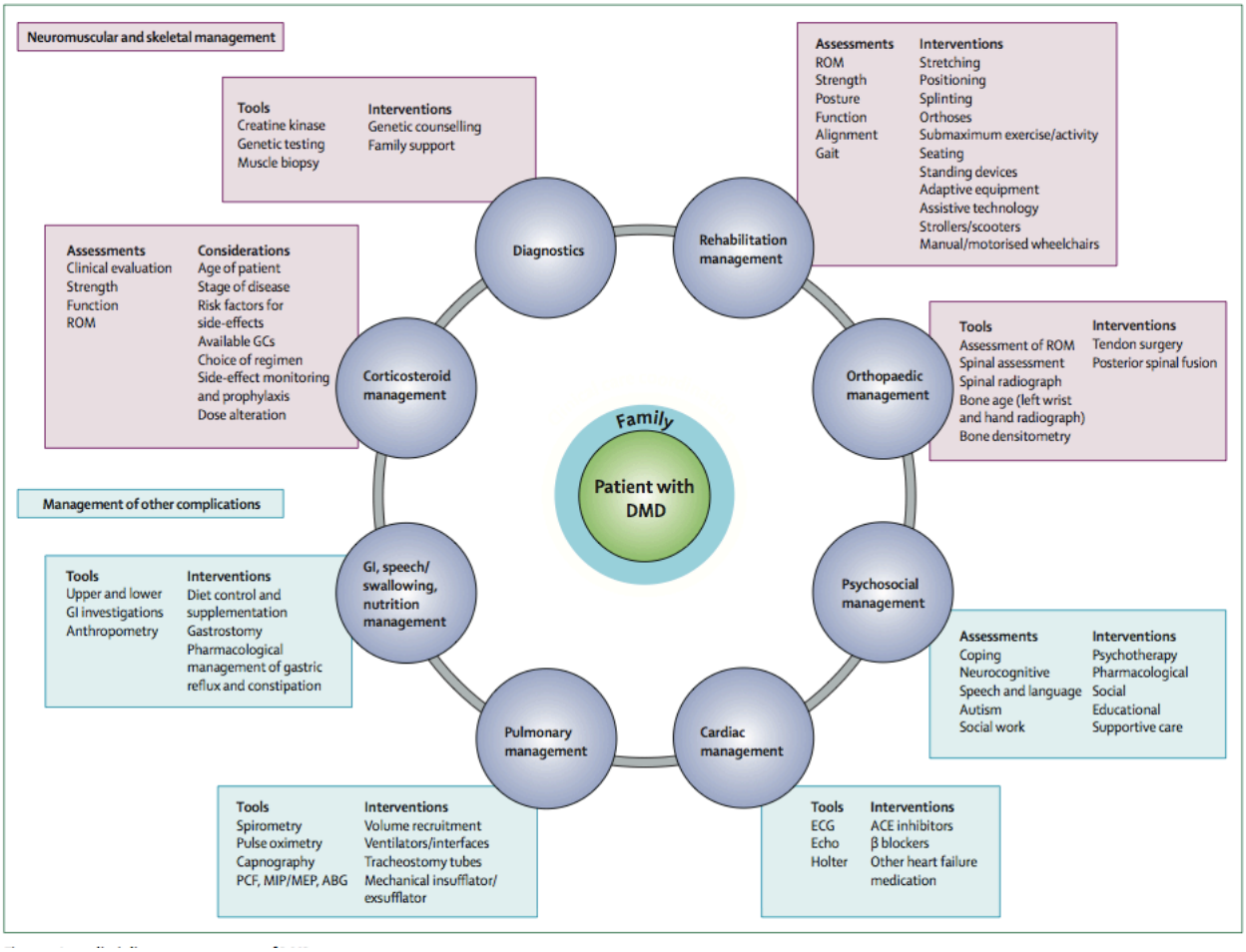


Figure 1: Interdisciplinary management of DMD
The core areas of management are shown above with the patient and family at the center of care. Figure from (Bushby et al. 2010a) and used with permission from Elsevier Limited.
ABG=arterial blood gas. ACE=angiotensin- converting enzyme. DMD=Duchenne muscular dystrophy. Echo=echocardiogram. ECG=electrocardiogram. GC=glucocorticoids. GI=gastrointestinal. MEP=maximum expiratory pressure. MIP=maximum inspiratory pressure. PCF=peak cough flow. ROM=range of motion.

3.3 IMPACT OF CHRONIC DISEASES AND DMD ON FAMILIES

The burden of having a child with disabilities can be significant for families. Approximately 20% of families with a child with special healthcare needs report that they have financial problems as a result of their child's needs (Kuhlthau et al. 2005; Chen and Newacheck 2006). Children with chronic health conditions, including muscular dystrophy, have been shown to

require anywhere from 2 to 20 times the costs for medical care when compared to the general population of children (Ireys et al. 1997; Kuhlthau et al. 2005; Ouyang et al. 2008). Such families are more likely to have out-of-pocket expenses related to their child's health needs (Anderson et al. 2007; Shattuck and Parish 2008).

Studies have associated having a child with special healthcare needs, including DMD, with diminishments in parental employment and mental health with increases in stress and distress (Polakoff et al. 1998; Kuhlthau et al. 2005; Bostrom et al. 2006; Chen and Clark 2007; Witt et al. 2009; Chen and Clark 2010; Kenneson and Bobo 2010). About 30% of families of children with special healthcare needs said they cut back or stopped working due to their child; this was likelier to be the case in lower income families (Chen and Newacheck 2006). Demographic characteristics associated with families with a child with a disability include lower, single income and higher likelihood to live in lower quality housing and in poverty (Anderson et al. 2007). Having a medical home, insurance coverage and access to community-based services are all associated with improved finance outcomes in these families (Kuhlthau et al. 2005; Chen and Newacheck 2006). A case-control study found higher risk for a depressive episode in parents of a child with DMD; single parenthood and older child ages were also found to be risk factors for distress and lower feelings of control in these parents (Abi Daoud et al. 2004).

The literature is replete with studies investigating quality of life, progression of clinical features and potential new therapies in DMD. There are few studies, however, attempting to depict the impact of DMD on families from an economic and healthcare utilization perspective. Compared to other common neuromuscular disorders, DMD was shown in one report to have the highest annual outpatient rehabilitative costs, the bulk of which came from wheelchair and other equipment needs (Koch et al. 1986). Chen et al found that family functioning was not

significantly correlated with the child's disability level, income or employment variables (Chen and Clark 2007).

Several recent studies have examined the socioeconomic burdens associated specifically with muscular dystrophy. Total medical care expenditures for a privately insured US population of families of a member (aged 30 or less) with muscular dystrophy were 13 times higher than a comparison population without muscular dystrophy (Ouyang et al. 2008). Another US study found that children with muscular dystrophy had more functional, emotional and behavioral problems as well as mobility and durable medical equipment needs than children with special healthcare needs without muscular dystrophy (Ouyang et al. 2012). Factors associated with being less likely to have a medical home in children with muscular dystrophy were being non-White, non-Hispanic; lower than high school parent education; income below the poverty line; no or public insurance; and single-parent household (Ouyang et al. 2012). Families of children with muscular dystrophy were more likely to be on public insurance; come from lower income and education households with financial problems and reduction in work hours; have more than 10 hours of care from family per week; and have out-of-pocket costs than children with special healthcare needs without muscular dystrophy (Ouyang et al. 2012).

3.4 HEALTHCARE UTLIZATION IN DMD

Several small studies, some of which are dated, have examined aspects of healthcare utilization and perceptions in DMD from the perspective of the family. Bothwell et al surveyed 31 families and found that treatments and issues related to preserving walking ability were most important, particularly in those with younger boys while those with older boys also felt that mental health

issues and services were very important (Bothwell et al. 2002). Arias et al surveyed 34 families of older males with DMD (ages 12 to 34) about palliative care services. They found that the majority of respondents had utilized respiratory care while 40% or less used nutrition, social work, or mental health services (Arias et al. 2011). Koch et al found that families who lived longer distances away from a Muscular Dystrophy Association (MDA) clinic (even with reimbursement for travel) tended to not make all their appointments and possibility underutilized available services (Koch et al. 1986). One of the major categories of problems U.K. parents of children with DMD experienced was in getting needed services and covering medical expenses as well as feeling dissatisfaction with services that were obtained (Firth et al. 1983). Another study found that patients and parents felt that psychosocial services and life expectancy information were important but felt this need was unmet; in contrast, healthcare providers at the same clinics reported more availability of such services (Madorsky et al. 1984). A Canadian study that included parents of children with DMD (as well as several other common chronic conditions) found that parents placed importance on providers' knowledge and interaction with their child; communications among providers about their child; and non-compartmentalization of services (Miller et al. 2009).

Recently, assessment of service and intervention use in families with DMD has been initiated through patient registries. DuchenneConnect, a registry created by Parent Project Muscular Dystrophy (PPMD), was started in late 2007 to "bridge the information gap between care providers, researchers and the patient community, thereby addressing medical care needs and accelerating the pace of therapeutic advancements" (Rangel et al. 2012). Parents and individuals with DMD, BMD, intermediate muscular dystrophies as well as carriers for these conditions can create a profile and give information on health services, devices, and medications

they use. As of the end of 2012, the registry had over 2,000 completed profiles (DuchenneConnect 2013).

The MDA announced plans in October 2012 to launch a national clinician-entered patient registry for three diseases, one of which is DMD, in 25 pilot clinics (Wolff 2012). A formal proposal was recently published in the journal *Neurology* (Scully et al. 2013). The registry aims to record clinical and health-outcome data from MDA clinic participants in the hopes of improving clinical practices, understanding of natural history and genotype-phenotype correlations and patient eligibility for clinical trials. A system of public reporting of clinic outcomes across MDA clinics is predicted to improve implementation and standardization of DMD care recommendations. This proposal cites the precedent set by the Cystic Fibrosis Foundation's registry system which has been credited with increased survival and improved outcome measures among patients (Scully et al. 2013).

Information from these registries is important for determining future directions needed in care. Transforming Duchenne Care (Cripe 2012; Kinnett 2012) is a PPMD initiative involving collaboration between PPMD and MDA with input from physicians, other healthcare providers and patient representatives. The initiative has the aim of promoting clinic transparency and adoption of DMD care recommendations and improving care delivery in North America. A long-term goal is to develop a Network of Duchenne Centers of Excellence based on consensus of an ideal model of care delivery for DMD along with insights gained from practices in the CF community, as mentioned above.

Similar efforts have been undertaken abroad. The European-based TREAT-NMD seeks to harmonize key clinical data (including some measures of medication and procedure use) from patients with confirmed DMD diagnoses in national patient registries into a global database

(TREAT-NMD 2013). Associated with TREAT-NMD is CARE-NMD, a collaboration of several European countries that seeks to enhance implementation of DMD care recommendations at care centers, assess patient quality of life and improve patient participation in national registries (CARE-NMD 2013). Alongside these efforts, focus has been aimed at determining what health indicators are useful in assessing quality of care in rare diseases, particularly in patient registries (EUCERD 2011).

3.5 NATIONAL INITIATIVE FOR FAMILIES WITH DUCHENNE (NIFD) SURVEY

The Cooperative International Neuromuscular Research Group (CINRG) is a consortium of medical and scientific investigators from academic and research centers facilitating neuromuscular disorder research. Founded in 1999, CINRG focuses on clinical research in DMD. Since then, the network has expanded to over 25 US and international sites and runs observational studies and clinical trials for neuromuscular disorders.

NIFD was developed in collaboration between researchers at Children's National Medical Center (CNMC) and Columbia University with funding from the CDC and American Association of Medical Colleges. As the first large-scale survey of DMD families in the US, NIFD was a lengthy cross-sectional survey developed to cover the following topics: family life (demographics, life events, home adaptation); child's health, medical care and schooling; diagnostic process; and impact on family (Figure A12). Families with a male child with DMD were eligible to take the survey. The aim of this survey was to capture what services families were receiving and the impact of DMD on their lives with the purpose of identifying gaps in DMD care and giving direction to future programs.

Data were collected between 2006 and 2009 from 235 respondents who took the survey in one of two formats: a paper version (n=121) and a web-based version (n=114). The paper version was completed as a baseline survey for US participants in CINRG's DMD Natural History Longitudinal Study: Relationship between Impairment, Activity Limitation, Participation and Quality of Life in Persons with Confirmed Duchenne Muscular Dystrophy (DMD), hereafter called the CINRG DMD Natural History study (McDonald et al. 2013). Given the significant impact of glucocorticoid treatment, this study was undertaken to provide an updated natural history for DMD. The study enrolled over 300 males ages 2 to 30 years with DMD from US and international sites. The goal is to generate the largest comprehensive longitudinal assessment of DMD by observing participants' physical abilities, quality of life, medical problems, healthcare utilization and genotype over a five-year period. Parents of participants had to be over the age of 18. The study began in 2006 and is currently continuing active protocol visits. The study excluded participants who were walking past the age of 13 (without glucocorticoids) or 16 (with glucocorticoids) and subjects/parents unwilling or unable to participate in the study's protocols and visits. Funding was recently received to extend the study for an additional three years. Enrollment has been re-opened to recruit a new young cohort of 4 to 7 year old boys with DMD and a healthy control group of males aged 6 to 30. Some of the first reports from this study are currently in press, including an article regarding study protocol and methods design (McDonald et al. 2013) and another regarding preservation of muscle and lung function with chronic use of glucocorticoids (Henricson et al. 2013).

4.0 MATERIALS AND METHODS

This project was reviewed by the University of Pittsburgh's Institutional Review Board and was determined to meet criteria for exemption (Appendix B). Data from the NIFD survey was received from the data manager at the CINRG Coordinating Center at CNMC. Data from the DuchenneConnect patient registry was received by formal request from the project's operations team.

4.1 DATA

4.1.1 NIFD Survey

Raw data collected from all NIFD survey respondents were obtained as a Microsoft Excel file after a formal data request to CINRG's Coordinating Center data manager. In total 235 surveys were completed between 2006 and 2009. The survey was completed in one of two formats: paper (n=121) or web-based (n=114). The NIFD paper survey was administered to US participants in the CINRG DMD Natural History study (n=116). An additional five respondents completed the paper version and mailed their survey to CNMC.

The remaining surveys (n=114) came from respondents who completed the survey on the Internet via posting at SurveyMonkey.com, an online survey tool. Participants accessed the

survey via announcements posted in MDA clinics and CINRG sites or by clinician invitation. It is possible they also may have found the survey on their own via Internet surfing. The method by which participants found the survey, however, was not assessed on the survey.

The population that took the Paper version of the survey (CINRG DMD Natural History study and five other respondents) is hereafter referred to as the "Paper" population while those respondents who took the survey at SurveyMonkey are referred to as the "Internet" population. Forty-four (18.7%) of surveys were excluded from final analysis due to non-response, duplicate respondents and more than one family member being represented (see details below in Methods). Overall, these exclusions resulted in a total of 191 respondents used in the final analysis (n=119 Paper respondents and n=72 Internet respondents).

4.1.2 Differences Between Internet and Paper versions of NIFD Survey

Overall, the differences between survey sections examined (Child's Health and Medical Care) in the Internet and Paper versions of NIFD were minimal. The biggest difference was that Internet respondents could complete portions of the survey more than once for each child with DMD that they had. These responses were excluded from analysis so that each respondent was only representing one child with DMD.

Because of the ability to enter information for more than one child, the order of sections on the Internet version differed from the Paper version, with Family and Diagnosis sections first and variables on Child's Health Status and Medical Care placed at the end of the survey. These latter sections were located at the beginning of the Paper version. In addition, Internet respondents were not able to complete the survey or proceed in the survey if they selected "No" to being willing to participate in the study, living in the USA, ever having a child diagnosed with

DMD or if they did not enter a US zip code or select a relationship to the child. Skip functions were not built into the Internet version for instances where a respondent entered “Yes” or “No” and subsequent questions depended on this first answer (i.e. “If yes,…” or “If no, why not?”). If a respondent selected “Other” for an option that had a “Specify” box to type in, the respondent was returned back to the page to enter a comment and typically could not proceed without specifying a typed answer or unchecking the “Other” category.

Other differences between the Paper and Internet versions included a pre-selected age or number ranges for questions eliciting an age or number of items/people on the Internet version. For example, on the Internet version, respondents could select “Less than 18”, numbers 18 to 70 or “Greater than 70” for Parent/Guardian age while those taking the Paper survey could write in two digits. Some wording differences or extra definitions were given and some questions had variations in the options respondents could select on certain versions of the survey (Table 1). In the case of different response options, the data from the Paper and Internet populations were harmonized so that the same categories and answer types were used in analysis of the data.

Table 1: Differences in NIFD Paper and Internet versions

Variable	Paper	Internet
Parent/ guardian questions	--	(If parents are divorced and/or remarried, please provide information about the parents/guardians who spend the most time living with the child.)
Racial Category	African American	African American/Black
	Caucasian	White / Caucasian
	Native American/Alaskan Native	Native American/Alaskan Native
	Asian or Pacific Islander	Asian
	--	Native Hawaiian/Pacific Islander
	--	Other (please specify)
Insurance plan for child (choose all that apply)	None	No insurance / Self-pay
	Self Pay	--
	HMO	HMO or managed care plan (where you see doctors who belong to a network)
	Other managed care plan (including preferred provider organizations (PPO's) and Point of Service (POS) plans).	--
	Traditional insurance plans (BlueCross/BlueShield, etc.)	Traditional insurance plans (where you see the doctor of your choice, and may have to apply for reimbursement)
	Medicaid/State-sponsored programs	Medicaid or government-sponsored programs
	Military	Military healthcare plan
	Don't know or don't remember	Don't know or don't remember
	Other (specify)	Other (specify)
Major expenses not covered	Durable medical equipment	Durable medical equipment
	Therapy (PT, OT, Speech)	Therapy (PT, OT, Speech)
	Mental Health Services/Counseling	Mental Health Services/Counseling
	Medicines	Medicines
	--	Other (specify)

4.1.3 DuchenneConnect Data

A PDF version of the DuchenneConnect registry questions was analyzed for similarity to questions from NIFD. To facilitate this process, a Microsoft Excel spreadsheet was generated to list side-by-side similar or same questions between the surveys along with the possible answers from each survey. A DuchenneConnect data request was created utilizing questions that were the same or that could be harmonized to NIFD's questions and submitted to the DuchenneConnect operations team. Data were requested for those with a diagnosis of DMD and living in the United States.

The data were received for 1201 registry profiles from 2007 to 2013 from the DuchenneConnect operations team. The data were shared in a Microsoft Excel spreadsheet with counts and percentages for each question requested. Additionally, counts for current age, gender and ancestral background for the total population were included.

4.2 METHODS

4.2.1 Exclusion of NIFD Surveys from Analysis

In total, 235 NIFD surveys were completed (n=121 Paper; n=114 Internet). Forty-four (18.7%) of surveys were excluded resulting in a total of 191 respondents in the final analysis (n=119 Paper population and n=72 Internet population). The details of the exclusion process are detailed below and in Figure 2.

Twenty-seven respondents from the Internet population were excluded from analysis because they did not respond to questions in the sections investigated in this study regarding Child's Health and Medical Care.

Nine surveys (n=1 Paper and n=8 Internet) were excluded because they represented duplicates, meaning respondents had already taken the survey at a different time for the same child. Duplicate responses were determined based on zip code, child's birthdate, race and ethnicity and parent/guardian ages and occupations. In determining which response set to keep, the two response sets for each respondent were analyzed for completeness first then for how recently the survey was completed (if both responses sets were similarly complete). The more complete or more recent surveys were kept. Five pairs of duplicate responses were from individuals who took both the paper version at a CINRG site through the DMD Natural History study and the Internet version at SurveyMonkey.com. The paper surveys were kept for four of these respondents owing to more completeness of answered questions or a more recent date of taking the survey. The Internet version of the fifth set of duplicate responses from this group was kept because it was more recent than the paper survey. The remaining four pairs of duplicate responses were from individuals who took the Internet version of the survey twice. In all four pairs, the more complete survey was kept for analysis.

Eight surveys (n=1 Paper and n=7 Internet) were excluded because respondents had completed the survey for more than one child with DMD in their family. In these cases, surveys completed for the oldest child with DMD were retained for analysis.

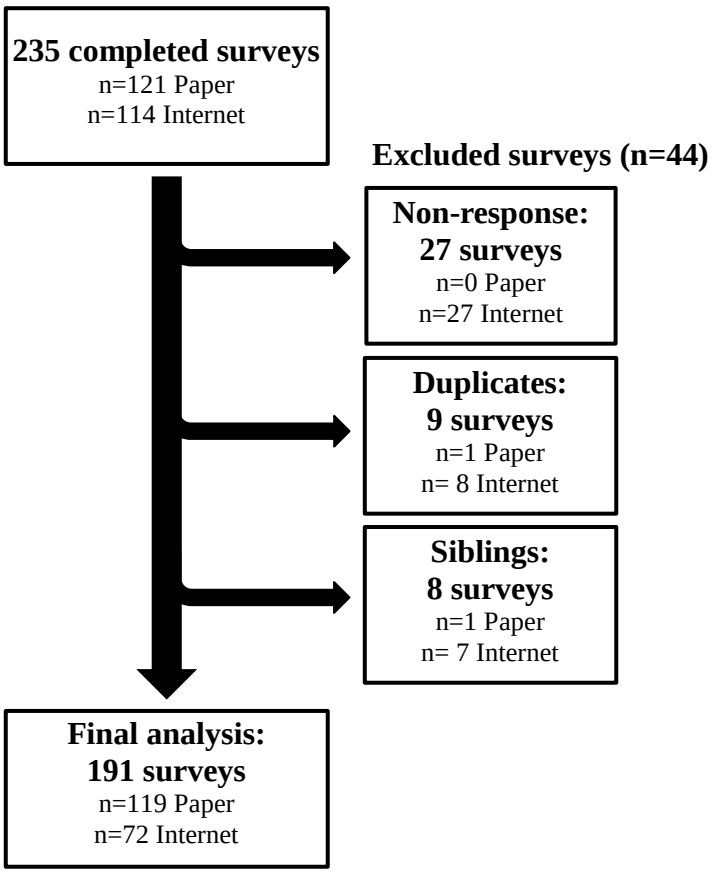


Figure 2: Inclusion process for completed surveys in final analysis
Non-response = no response in Child's Health and Medical Care sections; Duplicates = surveys taken two times by one respondent for the same child; Siblings = surveys taken by respondent who already took the survey for an older child in the family

4.2.2 Data Cleaning of NIFD Data

A data cleaning process was developed with the CINRG Coordinating Center data manager and performed on data in Excel files from survey sections pertaining to Child's Health and Medical Care. The overall philosophy was to minimize making changes to or assumptions about the data to preserve respondents' replies (and to avoid making a question unreliable) while noting skip patterns or unusual responses to questions. If a Yes/No question asking if a child used a service

or device was blank but information was entered in corresponding “If yes” questions or if an answer was entered for the “If no” question, the blank Yes/No variable was changed to “Yes” or “No”, respectively. Unusual or implausible answers or patterns were noted though not necessarily changed. For example, this would include a respondent who said their child took every type of heart medication listed. In addition, if a respondent wrote in an answer in an “Other, Specify” box that was already an available answer option, then the response was changed to the available answer option.

For the Internet population, the age at first doctor or health professional visit variables were determined to be unreliable due to entered ages exceeding the child’s current age. The data were received from the CINRG Coordinating Center with these conflicting values and were excluded from the analysis.

The date the survey was taken was used with the child’s birthdate to determine child’s age. For four Paper respondents, the date of survey was unable to be determined and a blanket date was estimated based on responses that elicited the child’s age at procedures or provider visits.

Scales used for responses between the Paper and Internet population were harmonized so that the same categorization of variables was used across both populations to address slight variations in the way answer options were listed. Because not all respondents answered every question, n values representing the total number of respondents specific to that question are given in the Results section.

4.2.3 NIFD Data Analysis

IBM's SPSS Statistics version 21 software package was used for analysis. For Aim 1, descriptive statistic functions were used to describe survey variables for the entire dataset as a whole (i.e. Paper and Internet populations combined). Categories were created for some variables to gain an overall picture of the data. For instance, categories for key age groupings based on standard disease course were created from child's age. For a question regarding walking ability, four categories were created by collapsing 10 possible responses into four similar groups. For some questions using ordinal responses measuring frequency, categories were combined. For instance, responses regarding worry or concern for the child's physical, emotional and behavioral health were grouped from five (None, A little bit, Some, Quite a bit, A lot) to three categories (None, A little bit/Some, Quite a bit/A lot). For questions where respondents could check all answers that applied, an additional variable was created to assess how many respondents selected at least one of the possible responses. Examples of these variables include: diagnoses other than DMD, major expenses not covered by health insurance, use of lung clearance and assisted ventilation devices.

For Aim 2, significant differences between Paper and Internet population demographic variables were analyzed using Fisher's exact 2-sided test (alpha set at 0.05) for categorical variables (e.g. respondent's relationship to child; parent/guardians' education and employment statuses; child's race and ethnicity) and independent-samples t-test of means (alpha set at 0.05) for scale variables (e.g. parent/guardians' ages and child's age).

To capture education and employment factors of the household or family unit representing each child, the highest education level and the combination of work statuses among parent/guardian pairs were generated. To analyze other non-demographic variables with more

than two possible answers between the two populations, dichotomous categories were created. For example, quality of healthcare responses were collapsed into two categories: “High quality” and “Less than high quality”.

Since multiple responses were possible on insurance plans several modifications were made to analyze differences between the populations. Eight respondents who selected no insurance types among all choices were considered as non-responses and excluded from analysis. For each plan type, respondents who did not select the type were coded as 0 (No) while coding for those who selected a plan (1) was retained.

For Aim 2, a partial correlation table controlling for survey population was generated and color-coded to identify associations between variables. Demographic, worry/limitations/satisfaction, child health status, healthcare quality and understanding, and selected provider variables were analyzed for associations with most variables examined in the survey sections under study (Child’s Health and Medical Care). A two-tailed significance p-value of ≤ 0.10 and correlation value ≥ 0.30 was considered significant.

Forward and backward linear regression models were generated for two dependent variables (frequency of pain/discomfort for the Paper population and overall life satisfaction for both populations). Data from the Internet population on frequency of pain/discomfort was not available. First, potential independent variables were selected by using those identified in the correlation table with significant correlations to the dependent variable. Second, to avoid including independent variables with correlations to each other in regression modeling, variables of interest that were also unrelated to each other were selected.

Using this approach, the following were set as independent variables for the outcome of frequency of pain/discomfort: child’s limitations due to health problems, use of albuterol for

strength, use of proton pump inhibitors, use of manual wheelchair, seeing a cardiologist and child's satisfaction with school ability. The following were set as independent variables for the outcome of child's overall life satisfaction: child's satisfaction with friendships, use of attention deficit disorder/attention deficit hyperactivity disorder (ADD/ADHD) medications, child's health other than DMD, walking independently and respondent's worry or concern regarding child's behavior. In addition, survey population was included as an independent variable for child's overall life satisfaction. Regression modeling p-values ≤ 0.10 were considered significant.

4.2.4 Harmonization of Data between NIFD and DC Populations

For Aim 3, data between the two surveys was first harmonized by generating comparable categories for similar questions. Demographic information on DuchenneConnect data included current age, gender, and racial background. Thus it was not possible to determine if DC respondents were related to each other or how other demographic factors compared between the NIFD and DC populations. It was also not possible to determine if there were respondents who completed both the NIFD and DC profiles.

DC data included the first choice selected by participants for one question on racial/ethnic background. NIFD racial and ethnic data (originally two separate questions with only one answer allowed) were combined into one variable to match that of DC, whose survey had Caucasian/Hispanic and Caucasian/Not Hispanic among other possible responses. Combining these NIFD variables excluded five respondents who specified either race or ethnicity but not both (e.g. Caucasian with no response on Hispanic origin; Hispanic or non-Hispanic with no race selected).

Co-occurring diagnoses other than DMD were compared. There were differences in wording of some conditions. For example, “global developmental delay” and “speech/expressive language delay” on DC versus “developmental delay” and “speech delay” on NIFD. There were also a larger number of diagnoses queried on the DC profile. Similarly, for medical expenses, NIFD respondents who had health insurance for their child were asked “what major expenses have not been covered by the plan” versus DC participants who were asked about expenses they have “problems getting reimbursed by insurance or obtaining approval”. Data for these questions was compared for “Medications” and “Durable Medical Equipment” (NIFD) and “Medicines” and “Devices or equipment” (DC).

To harmonize insurance type data, DC data for “Medicaid” and “Medicare/Medicare advantage” were combined to compare to NIFD’s “Medicaid/State sponsored programs” count. Similarly, DC data for “Private/individual” and “Commercial/employer” were combined to compare to a combined count of NIFD’s “Traditional insurance plans” and “HMO/Other managed care plan”. “No insurance” (DC) and “No insurance/self-pay” (NIFD) and “Military” (same for both surveys) categories were directly compared between populations. An “Other” category was created for both populations. For DC this included selections of “Prefer not to answer”, “National Health Programs” and “Other US federal programs”. For NIFD, the “Other” category included an “Other” option from the survey.

Walking ability data from NIFD were harmonized with DC’s response categories for how participants get around outside the home. NIFD respondents could select one of eleven possible choices for typical walking ability that touched on walking in and outside home. Seven of these choices ranging from “Cannot take any steps at all (primarily uses power wheelchair)” to “Walks for 15-50 feet but only inside at home” were coded as DC’s “I use a wheelchair or other

mobility device and rarely or never walk". Three NIFD choices indicating ability to walk outside the home with varying requirements for assistance were coded as DC's "I get around without a wheelchair or scooter but I need help". The remaining NIFD choice indicating full walking ability without assistance was coded as DC's "I usually walk on my own and I don't need help or assistive devices".

Use of therapies, equipment and medications was directly compared for the most part between NIFD and DC data. For glucocorticoid use, NIFD respondents reporting their child's use of at least one of prednisone, prednisolone or deflazacort were included in a "Glucocorticoids used" category. Similarly, DC respondents who reported they were currently using deflazacort or prednisone or who reported past use of glucocorticoids were included in a "Glucocorticoids used" category. The DC profile asked about current use of wheelchair types (choose all that apply) whereas NIFD asked if patients had ever used these devices. To harmonize to DC data, NIFD data on manual and power wheelchair use were combined into one variable. Those who only reported having used a manual wheelchair were coded as manual wheelchair while those who reported having used a power wheelchair only or both manual and power were coded as power wheelchair. This assumed for both datasets that an individual would not use a manual wheelchair once they had used a power wheelchair. Use of splinting was compared between the two surveys, which used different terminology for the same device: "night splints" on NIFD versus "AFOs (ankle-foot orthotics)" on DC. Lastly, to harmonize to DC's question regarding use of any breathing devices, a variable capturing use of at least one breathing device was generated for NIFD data. DC data on three different Bi-PAP usage scenarios was collapsed into one variable to reflect overall use of a Bi-PAP device.

4.2.5 DuchenneConnect Data Analysis

For Aim 3, descriptive statistics were generated for the DuchenneConnect population. For most DC variables, data on how many total participants responded to a question were not available. Therefore, for these questions percentages were generated by dividing total respective survey population (N=1201) by the total count of a particular variable. This same method was used on NIFD data when comparing variables between populations.

Respondents for both surveys were able to select as many insurance types that applied. Because several insurance types were combined for harmonization of data, these responses were analyzed by examining percentage of insurance types selected among the total number of selections made by respondents. Significant differences between population variables were determined by Fisher's exact 2-sided test or independent-samples t-test of means, both with alpha set at 0.05. The t-test was performed using SPSS software. Fisher's tests were calculated using an online calculator available from GraphPad Software at http://graphpad.com/quickcalcs.

DuchenneConnect collects date of birth, gender, and racial/ethnic background as part of an account registration that is separate from the patient's profile containing questions regarding use of services, medications and equipment. There were 23 DC registrants in a lumped age greater than 40 years category and 22 with reported female gender. Consultation with the DuchenneConnect Coordinator indicated that these responses are likely from parents (of a person with DMD) who filled out account registration with their personal date of birth and gender but filled out the patient profile section with their son's information. Thus, the ages greater than 40 years category was excluded in calculating descriptive statistics on age of individuals with DMD from the DC population. Gender was also assumed to be male for the DC population.

5.0 RESULTS

5.1 DESCRIPTION OF NIFD DATASET

Summary statistics were described for survey questions regarding demographics; health status of the child with DMD; general healthcare usage and quality; use of providers, services, equipment, medications, complementary/alternative medicine and procedures; and worry, satisfaction, limitations due to DMD. A subset of variables is described below. The remaining data description is located in Appendix C.

5.1.1 Demographics

The majority (79.7%; n=149) of survey respondents were biological mothers. Other relationships selected by respondents are shown in Figure 3. In the "Other "category, there was a sister and one individual with DMD who completed the survey by himself. There were no respondents who selected foster mother, stepfather or stepmother.

The survey elicited age, education and employment status for two parents/guardians (n=382 possible responses). The combined average age of both parents/guardians was 42.2 years (SD ± 8.5; range 20 to 66 years; n = 359). Among both parents/guardians, 40% had a bachelor's degree, some graduate schooling or held a graduate or professional degree. The majority were

working full time. Roughly half of families' annual income was less than or equal to $74,999. The distribution of parent/guardian ages and other demographic variables are shown in Table 2.

The mean age of the children with DMD for whom the survey was taken was 11.2 years (SD ± 6.1; range 1 to 28 years; n = 189). The median age was 10 years. Almost 70% of children had used glucocorticoids. The distribution of ages and glucocorticoid use are shown in Table 3. Most children were Caucasian and non-Hispanic background (Table C17).

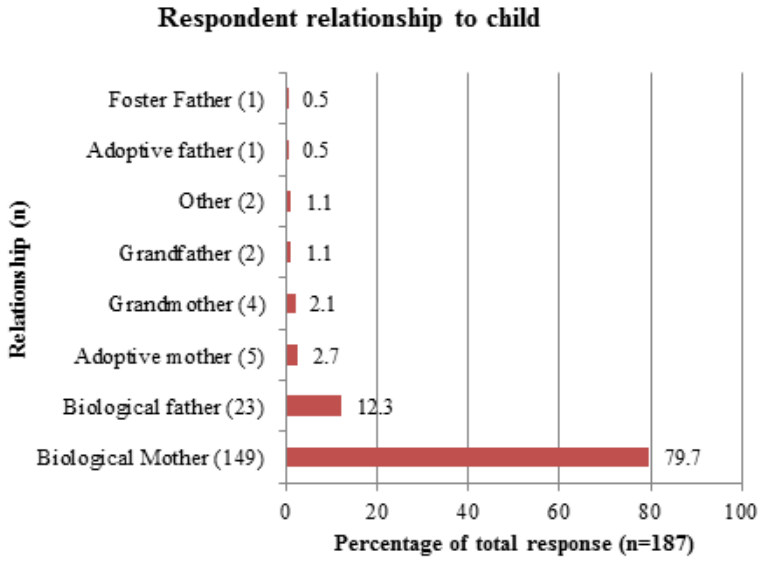
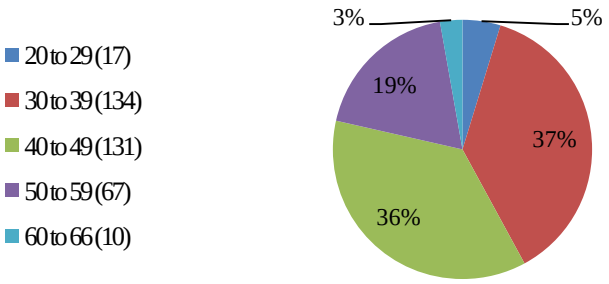
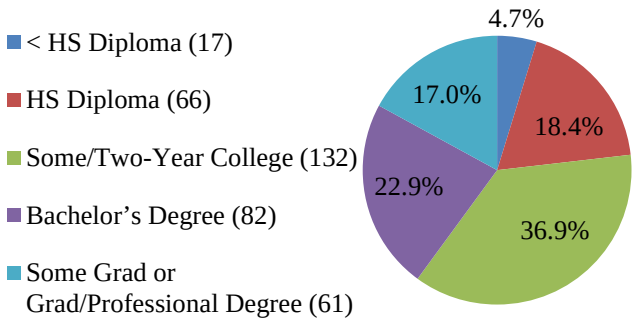
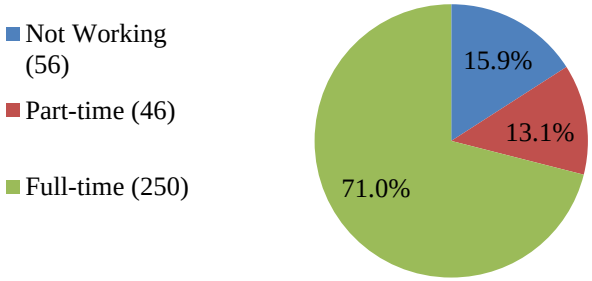
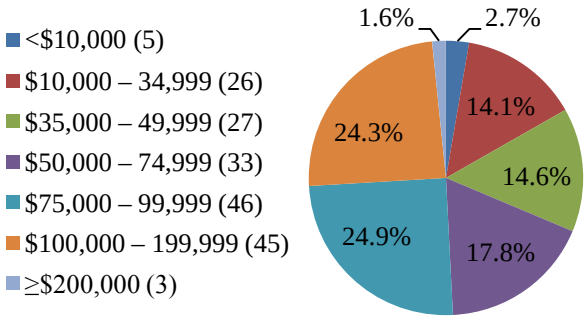


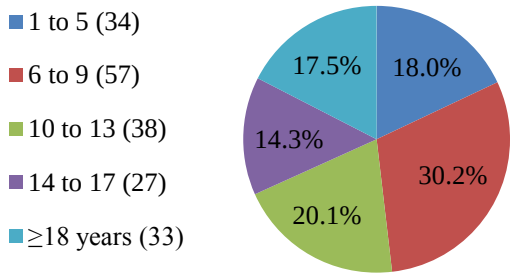
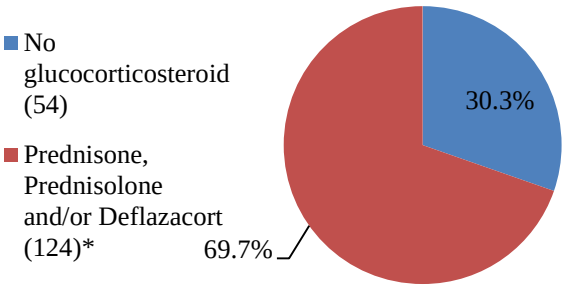
Figure 3: Respondent's relationship to child

Table 2: Respondent and Family Demographics

Demographic	Characteristic
Parent/Guardians' Age*, range in years (n) (total n=359)	
Parent/Guardians' Education* (n) (total n=358)	
Parent/Guardians' Employment* (n) (total n=352)	
Annual Family Income (n) (total n=185)	

* Respondents were able to enter age, education and employment status for two parent/guardians. Total possible n for combining these two variables =382.

Table 3: Child Demographics

Demographic	Characteristic
Child Age, range in years (n) (total n=189)	
Glucocorticoid Use (n) (total n= 178)	

* Respondents selecting "Yes" to the question "Has your child used the following" for at least one of the medications

5.1.2 Health Status of Child with DMD

Among 189 respondents, 57.1% (n=108) said their child was able to walk independently. Of 184 respondents who selected a statement that best summarized their child's typical walking ability, 38.1% (n=70) said their child was not able to take any steps at all and primarily used a power or manual wheelchair. 11.4% (n=21) could only walk for varying short distances in the home or at school with assistance. 41.3% (n=76) were able to walk outside the home but with varying levels of assistance. Meanwhile, 9.2% (n=17) said their child walks, runs and climbs without difficulty or assistance.

Respondents were asked to select how often their child experienced pain or body discomfort during the past month (Figure 4). Data were only available for this question from the

Paper population. Almost 75% experienced bodily pain or discomfort during this time period; about a third experienced it weekly or daily. Respondent's rating of the quality of their child's health other than the diagnosis of DMD are shown in Figure 4. Over 75% of children felt their child's health was excellent or very good. No respondents selected "Poor" for this question.

Respondents were able to select "Yes", "No" or "Don't Know" for each of nine conditions other than DMD that their child had been diagnosed with by a doctor or other professional. Of 189 respondents, about 57% (n=109) said their child had been diagnosed with at least one of these nine conditions. Data from respondents who answered "Yes" for the conditions are shown in Figure 5. Respondents were also able to select "Other" and specify an additional condition (Table C18).

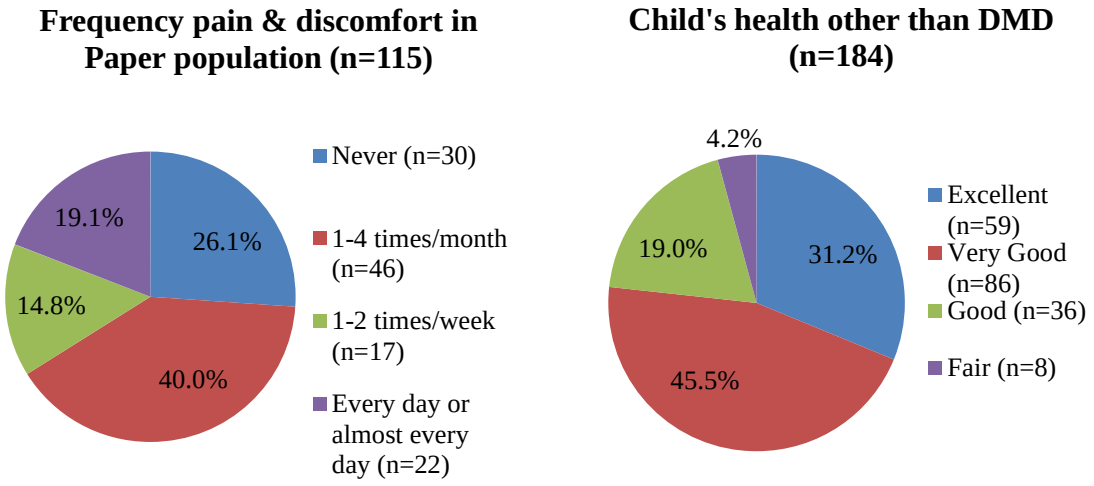


Figure 4: Child's pain frequency and health other than DMD
Left: Frequency of bodily pain or discomfort in the past month among Paper population (n=115); *Right*: Rating of child's health other than DMD in both populations (n=184)

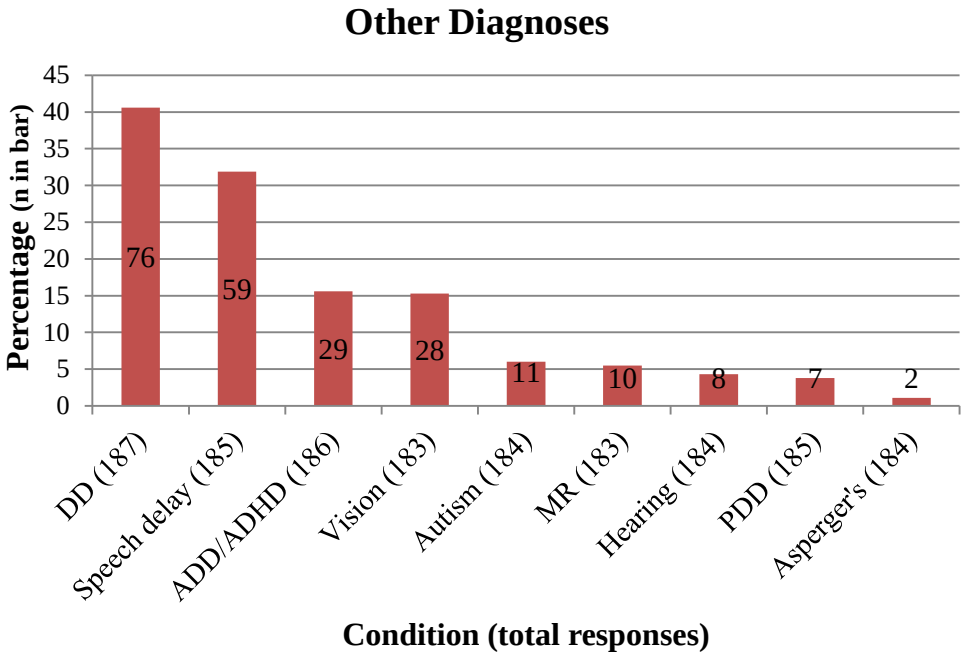


Figure 5: Diagnoses other than DMD
Respondents could select "Yes", "No" or "Don't know" for 9 conditions in response to the question "Have you ever been told a doctor or other professional that your has…". Data shown above are for those who responded Yes for each condition. Total number of responses for each diagnosis are shown in bars. DD = Developmental delay; ADD/ADHD = Attention deficit; Vision/Hearing = Impairment; MR = Mental retardation; PDD = Pervasive developmental disorder

5.1.3 General Healthcare Coverage, Understanding and Quality

Health insurance plans for the child with DMD are shown in Figure 6. Respondents could select as many plans types as applied. Thirty-seven to 44% of respondents (n=67-80) selected traditional, HMO/other managed care plans and/or Medicaid/State program plans. Two to 4% (n=4 to 7) selected None/self pay, Other and/or Military plans. For those with health insurance for their child, respondents were asked to select as many major expenses that were not covered by the plan as applied from a prescribed list. 84 respondents (44%) from the total survey population (N=191) selected as least one expense that was not covered (Figure 7). Over two-thirds of the selections made by this group were related to durable medical equipment and therapy (PT, OT, Speech) expenses.

To assess perceived knowledge of DMD, respondents were asked, “How well do you think you understand how DMD is inherited, whether future children might inherit it and the kinds of service needed?”. Over 60% (n=115) felt they knew these aspects of care very well while 34% (n=65) felt they knew somewhat well (Figure 8). The survey did not ask questions about DMD to assess actual knowledge of these areas.

Since the child’s diagnosis with DMD the overall quality of healthcare received by the child is shown in Figure 8. Over half of respondents felt their healthcare was high quality. Respondents were able to write or type in additional comments about the quality of healthcare received by their child since diagnosis. Forty-four respondents (23% of the total survey population) gave comments, which are detailed in Appendix C.3.2. Several themes emerged from respondents’ comment including praise for care, dissatisfaction with clinic logistics and/or doctors, and difficulty getting access to particular therapies.

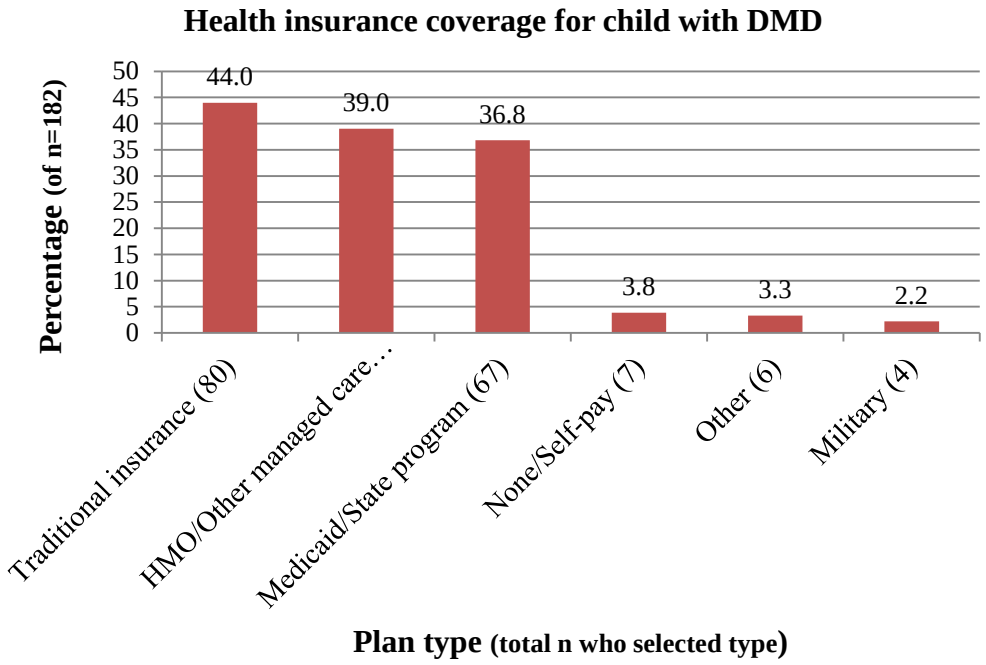


Figure 6: Health insurance plans for child with DMD
Shown are responses from 182 respondents who were able to choose all health insurance plans that applied to their child.

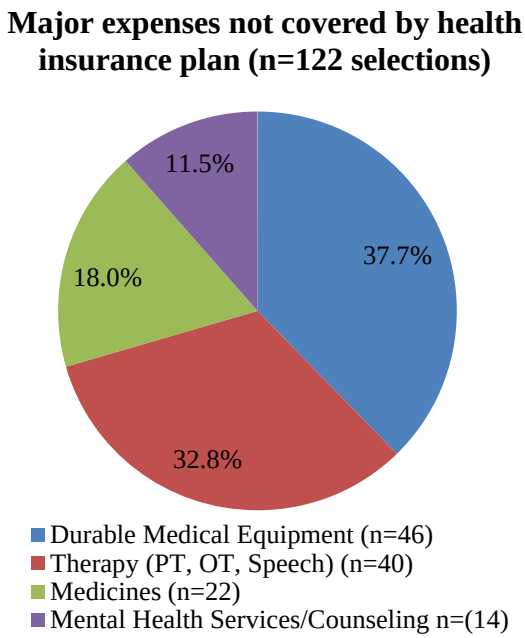


Figure 7: Major expenses not covered by health insurance plan
Respondents could select as any of the expenses types that applied. Shown are the percentages of 122 selections of major expenses not covered that were selected by 84 respondents (44% of total survey population). PT = physical therapy; OT = occupational therapy.

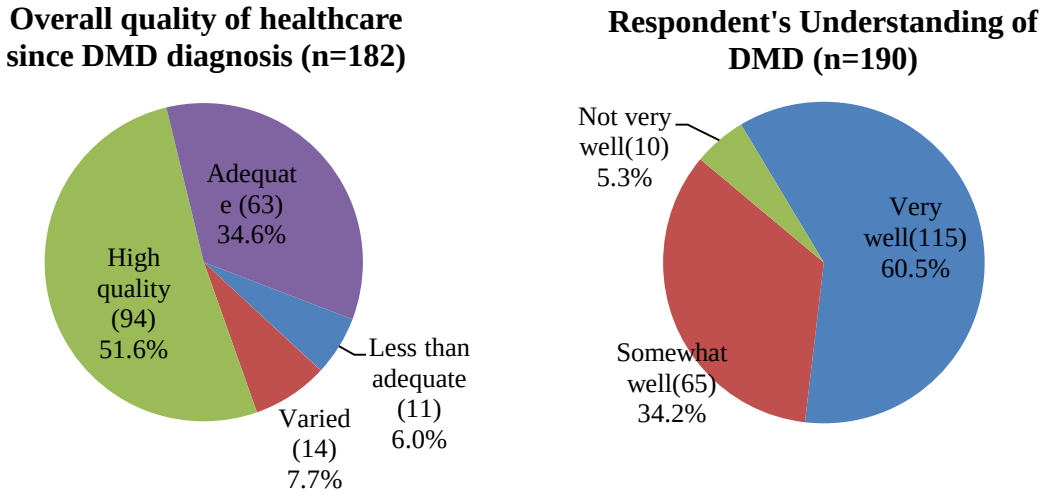


Figure 8: Overall quality of healthcare and respondents' understanding of DMD

5.1.4 Healthcare Providers

A multidisciplinary approach for care was suggested in that most children saw a neurologist followed by a large percentage seeing a cardiologist, pulmonologist and physical therapist outside of school (Table 4). Other providers seen are shown in Table 4. The age at first visit in years is shown for the Paper population for selected providers (Table 5); responses from the Internet population for this question were excluded from analysis due to unreliability of data (see Methods, Data Cleaning). Mean ages at first visit for the neurologist and physical therapist were 5 and 6 years, respectively. Mean ages at first visit for the cardiologist and pulmonologist were older at 9 and 11 years, respectively.

Reasons why children did not see a particular doctor or health professional are shown in Table 6 and Figure 9 for selected providers. For all providers, the largest percentage of respondents selected the reason "Child does not need this service". About 75% or more of these children were ages six years and older (Table 7). A handful of respondents' children in these tables may have seen the provider in the past based on concomitant responses of "Yes" to seeing the provider and/or giving the age of the child at first visit; thus their responses in the table may reflect why their child was not currently seeing that provider despite having seen them in the past.

Respondents were asked in a separate section of the survey if a genetic counselor or geneticist helped "define your risk of having additional children affected by DMD". Using this question as proxy for seeing these providers, 61.1% (n=113) of those who responded to this question (n=185) saw a genetic counselor or geneticist.

Table 4: Doctors or health professionals seen by child

Doctor or Health Professional*	Count (Yes)	Count (No)	Total Response [a]	Percentage (Yes/Total Response)
Neurologist	154	28	182	84.6
Cardiologist	129	52	181	71.3
Pulmonologist	94	85	179	52.5
Physical therapist [b]	90	91	181	49.7
Nutritionist	48	131	179	26.8
Physiatrist	46	132	178	25.8
Occupational therapist [b]	45	133	178	25.3
Social worker	41	139	180	22.8
Gastroenterologist	29	149	178	16.3
Mental health therapist	29	151	180	16.1
Speech therapist [b]	15	162	177	8.5

* Respondents were asked "Does your child see the following doctor or health professional? (Yes/No)"

[a] Total response from 191 possible respondents

[b] therapist seen outside of school

Table 5: Age at first provider visit for selected providers (Paper population)

Provider	Mean Age, years ± SD *	Range (years)	Total responses Age at visit	% (n) seeing doctor (of n=119)
Neurologist	5 ± 3	<1 - 20	79	76.5 (91)
Cardiologist	9 ± 5	<1 - 23	78	68.1 (81)
Pulmonologist	11 ± 5	2 - 22	58	51.2 (61)
Physical therapist [a]	6 ± 3	1 - 18	43	40.3 (48)

* Respondents were asked "How old was your child at the first visit" and could write in year and month values; only year values are shown. Data were only analyzed for the Paper population (total population= 119).

[a] therapist seen outside of school

Table 6: Reasons why child did not see selected providers

Provider*	Total response	None available % (n)	Too expensive % (n)	Concern about medical insurance % (n)	Child does not need this service % (n)	Other % (n)
Neurologist	25	8 (2)	0 (0)	0 (0)	68 (17)	24 (6)
Cardiologist	45	2.2 (1)	0 (0)	0 (0)	77.8 (35)	20 (9)
Pulmonologist	77	2.6 (2)	0 (0)	0 (0)	72.7 (56)	24.7 (19)
Physical therapist [a]	78	12.8 (10)	12.8 (10)	14.1 (11)	32.1 (25)	28.2 (22)

* "Religious reason" was an additional answer option but no respondent selected this answer for any provider type

[a] therapist seen outside of school

Table 7: Age at time of survey for children who did not see a provider due to not needing the service

Provider	% (n) by age category of those who did not see a doctor for the reason "Child does not need this service"						Total count % of total survey population (N=191)
	1 to 5 years	6 to 9 years	10 to 13 years	14 to 17 years	≥ 18 years	Total Count	
Neurologist	0 (0)	47.1 (8)	17.6 (3)	11.8(2)	23.5(4)	17	8.9
Cardiologist	26.5 (9)	50 (17)	14.7 (5)	2.9 (1)	5.9 (2)	34*	17.8
Pulmonologist	23.6(13)	49.1(27)	21.8(12)	1.8 (1)	3.6 (2)	55*	28.8
Physical therapist [a]	4 (1)	44 (11)	20 (5)	4 (1)	28 (7)	25	13.1

* Totals do not equal those in Table 6 above because respondent did not give child's date of birth.

[a] therapist seen outside of school

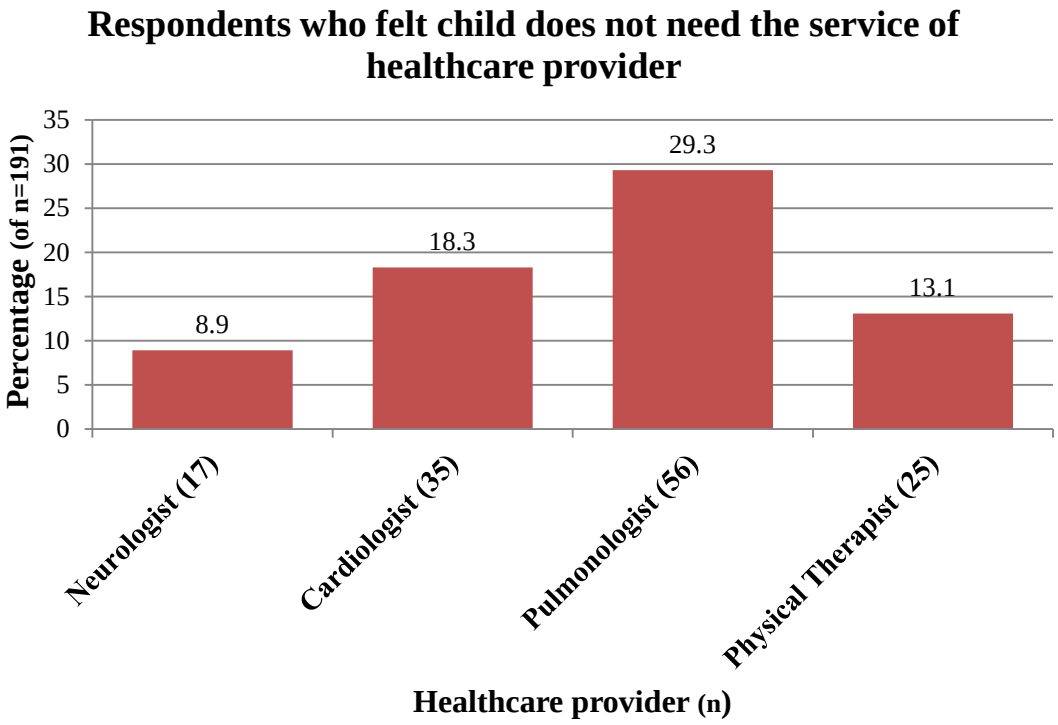


Figure 9: Respondents who felt their child does not need the service of healthcare providers

5.1.5 Durable Medical Equipment and Devices

About 46 to 61% (n=83 to 111) of children had used power wheelchair, manual wheelchair and/or night splints while much less used lung clearance and assisted ventilation devices (Table 8). The percentage of children in each age category using selected durable medical equipment is shown in Table 9. A large jump in percentages occurred between the 6 to 9 and 10 to 13 age groups for both wheelchair types. All individuals with DMD aged 18 and older were using a power wheelchair while 55 to 58% (n=18 to 19) were using respiratory devices. In this table, data are shown for those who responded both to child's age at the time of survey and to use of equipment questions.

Table 8: Equipment and breathing device use

Device*	Count (Yes)	Total Response [a]	Percentage (Yes/Total Response)
Night splints	111	183	60.6
Manual wheelchair	94	182	51.6
Power wheelchair	83	180	46.1
Lung clearance devices [b]	33	179	18.4
Assisted ventilation devices [c]	28	179	15.6

[*] Respondents were asked "Has your child used the following? (Yes/No)"

[a] Total response from 191 possible respondents

[b] Respondents who selected at least one lung clearance device from 5 types (Emerson cough assist, Vortran percussive nebulizer, intrapulmonary percussive ventilation, Thera vest, chest percussion)

[c] Respondents who selected at least one assisted ventilation device from 6 types (Bi-PAP, tracheotomy, C-PAP, mouthpiece/Sip n Puff, cuirass, negative pressure)

Table 9: Percentage of children in age category who have used equipment or device

Equipment/Device	% (n) of total children in age category who have used device*					
	1 to 5 (n=34)	6 to 9 (n=57)	10 to 13 (n=38)	14 to 17 (n=27)	≥ 18 (n=33)	Total Count for device
Night splints	23.5 (8)	71.9 (41)	57.9(22)	77.8 (21)	54.5 (18)	110
Manual wheelchair	2.9 (1)	29.8 (17)	71.1 (27)	85.2 (23)	78.8 (26)	94
Power wheelchair	0.0 (0)	8.8 (5)	57.9 (22)	85.2 (23)	100 (33)	83
Lung clearance devices [a]	2.9 (1)	3.5 (2)	2.6 (1)	37.0 (10)	54.5 (18)	32
Assisted ventilation devices [b]	0.0 (0)	1.8 (1)	2.6 (1)	25.9 (7)	57.6 (19)	28

[*] Shown are those who selected "Yes" to use of equipment type (n varied) and gave their child's age at the time of survey (n=189). Percentages were calculated using the total "Yes" responses for an age category divided by the total number of children from the survey in the age category.

[a] as above for b in Table 8

[b] as above for c in Table 8

5.1.6 DMD's Impact: Worry, Limitations and Satisfaction

Respondents were asked several questions about the impact that aspects of DMD had on them or their child in the month before completing the survey. One such question asked how much emotional worry or concern did their child's physical health, emotional well-being and behavior

caused them with “None”, “A little bit”, “Some”, “Quite a bit” and “A lot” as possible answers. To aid in analysis, these questions were collapsed into three categories with “None” as its own category; “A little bit” and “Some” combined into a second category and “Quite a bit” and “A lot” combined into a third category. About 44% , 38% and 22% of respondents reported quite a bit or a lot of worry or concern for their child’s physical health, emotional well-being and behavior, respectively (Figure 10).

Limitations in the child’s schoolwork or activities with friends due to problems with health, emotional difficulties and behavioral difficulties in the past month were rated by respondents with “No, not limited”, “Somewhat limited” and “Yes, very limited” answers. (Figure 11). The majority of parents did not report that their child experienced limitations due to health, emotional, or behavioral difficulties in the past month.

Lastly, respondents rated how satisfied they thought their child felt about life overall in the past month with “Very satisfied”, “Somewhat satisfied”, “Not satisfied/Not dissatisfied”, “Somewhat dissatisfied” and “Very dissatisfied” as answer options. About 80% (n=149) of respondents thought their child felt very satisfied or somewhat satisfied with life in the past month (Figure 12).

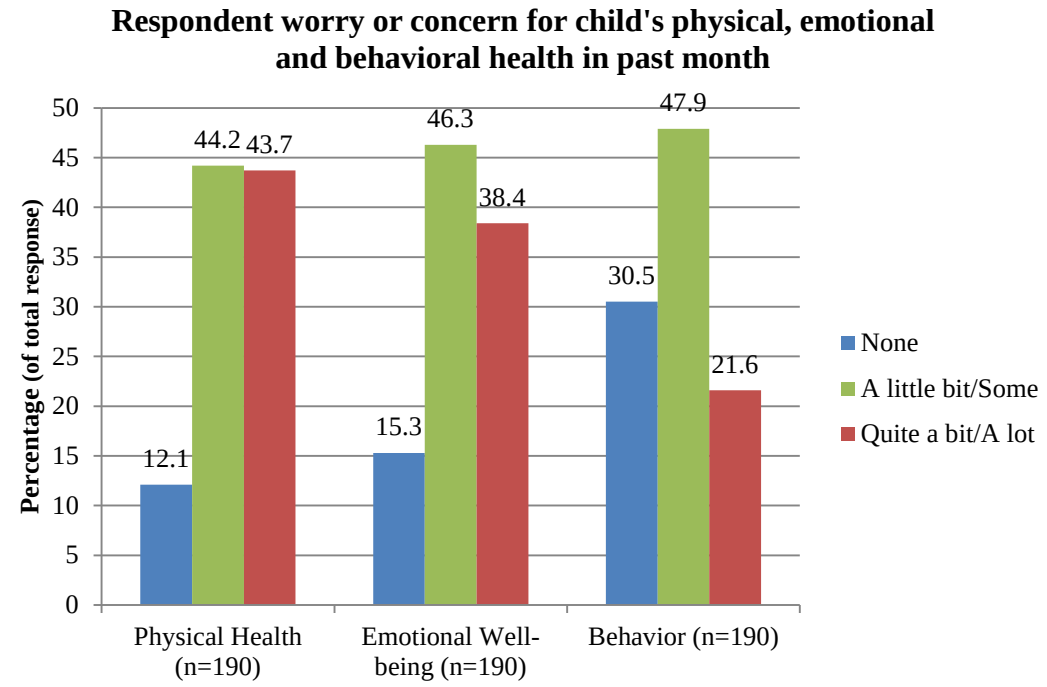


Figure 10: Respondent worry or concern for child's physical, emotional and behavioral health in past month

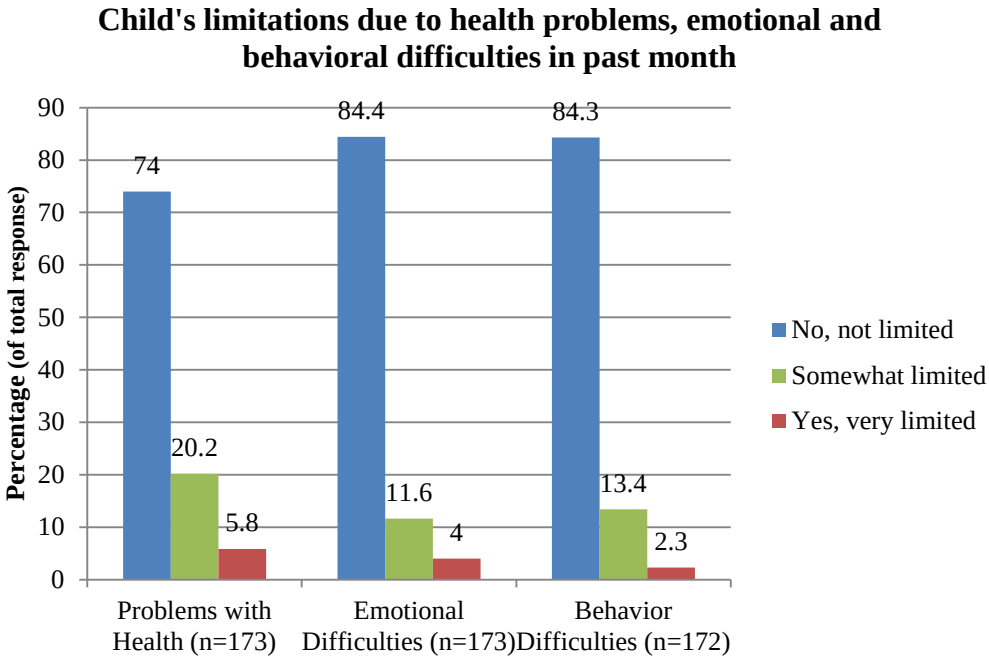


Figure 11: Child's limitations due to physical, emotional and behavioral difficulties

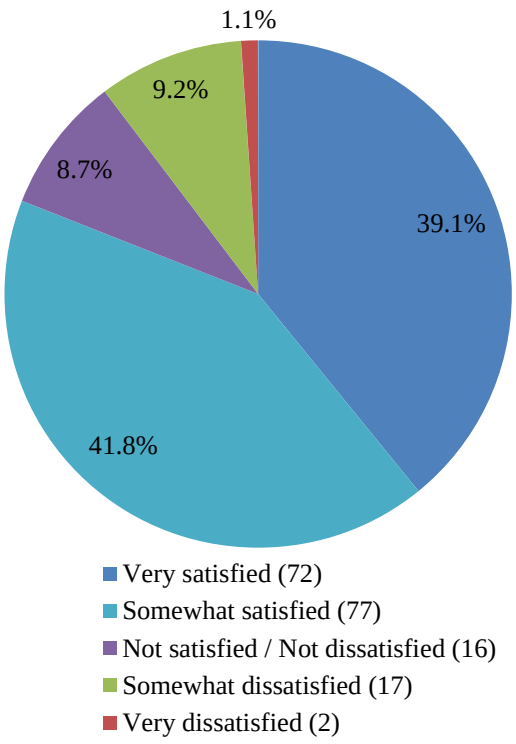


Figure 12: Child's overall life satisfaction in past month

5.2 DIFFERENCES BETWEEN PAPER AND INTERNET NIFD POPULATIONS

Because the NIFD population was composed of two populations (one who took the survey in paper format and the other who took a web-based survey posted on the Internet) analysis for significant differences between population demographics was performed. Based on the differences uncovered, selected variables were analyzed between these populations.

5.2.1 Demographic Factors

Demographic factors were significantly different between the two populations for child's age, combined age of parents/guardians, highest parent/guardian education level, and annual family income (Table 10).

The mean age of the parents/guardians and age of the child among the Internet respondents was lower than that of the Paper respondents. For the Internet population, child ages ranged from 1 to 20 years and mean parent/guardian ages ranged from 24 to 58 years. For the Paper population, child ages ranged from 2 to 28 years and 20 to 66 years for parent/guardian ages. The percentage of parents/guardians aged 40 and over was 63.1% (142 of 225 responses) for the Paper population versus 49.3% (66 of 134 responses) for the Internet population. For child's age, 51.7% (61 of 118 responses) of the Paper population were aged 12 and over versus 28.2% (20 of 71 responses) of the Internet population. Both of these differences were significant by Fisher's 2-sided exact test at $p = 0.011$ for parents' age and $p = 0.002$ for child's age.

The highest level education level achieved between parent/guardian pairs was higher in the Internet population with about 61% (n=43) having a bachelor's degree or higher versus 39% (n=46) achieving this level in the Paper population. Annual income was also higher in the Internet population with 80% (n=56) have annual incomes equal to or greater than $50,000 versus 67% of the Paper population with this income level.

Table 10: Demographic differences between Paper and Internet populations

Demographic Factor	Population				P-value
	Paper	Paper response (of n=119)	Internet	Internet response (of n=72)	
Relationship to child: Biological Mother % (n)	80 (92)	115	79.2 (57)	72	1.0 [c]
Parent/Guardian Ages mean in years ± SD	43.3±8.9	225*	40.4±7.2	134*	**0.001**[d]
Highest parent/guardian education level [a]: ≥ Bachelor's degree % (n)	39.3 (46)	117	61.4 (43)	70	**0.004**[c]
Employment [b]: Two full-time working parent/guardians %(n)	42.7 (50)	117	44.1 (30)	68	0.879[c]
Annual income: ≥$50,000 %(n)	61.7 (71)	115	80 (56)	70	**0.009** [c]
Child Age: mean in years ± SD	12.6±6.4	118	8.8±4.5	71	**<0.001**[d]
Child glucocorticoid use % (n)	71.4 (85)	119	66.1 (39)	59	0.492[c]
Child's Race:White/Caucasian %(n)	92.2 (107)	116	97.1 (66)	68	0.217[c]
Child's Ethnicity:Not Hispanic %(n)	96.5 (110)	114	94.4 (67)	71	0.485[c]

* Respondents were able to enter values for two parents or guardians; total possible n for Paper = 238 and n for Internet = 144

SD = standard deviation

a Parent education was determined by counting the highest education level between parent/guardian pairs (or education level of single responses in the case that a second education level for a second parent/guardian was not given) for each represented child.

b Categories for family employment status were generated from combinations of three possible responses (full-time, part-time, not working) for two parents/guardians (e.g. 2 full-time workers;1 full-time + 1 part-time; etc.).

c Fisher's exact 2-sided test; values in bold are significant at alpha ≤ 0.05

d Independent samples t-test; values in bold are significant at alpha ≤ 0.05

5.2.2 Other Variables

Given these demographic differences, the distributions of other survey variables were compared between populations. Variables examined were: independent walking; one or more other diagnoses; insurance plans; one or more non-covered medical expense; quality of healthcare since diagnosis; respondent understanding of DMD; seeing a neurologist, cardiologist, pulmonologist, physical therapist; use of night splints, manual & power wheelchairs, lung clearance devices, assisted ventilation devices; child's overall life satisfaction and limitations due

to health problems. To facilitate testing for significant difference between variables, some modifications were made to variable categories as described in Methods.

Five variables with significant differences between populations were found (Table 11). Ability to walk independently was less in the Paper population, which also had higher use of power wheelchair and assisted ventilation devices. Higher percentages of the Internet population saw a neurologist and physical therapist outside of school.

Table 11: Significant differences in ambulation and healthcare variables between Internet and Paper populations

Variable	Population				P-value [a]
	Paper % (n)	Paper response (of n=119)	Internet % (n)	Internet response (of n=72)	
Walking independently	45.8 (54)	118	76.1 (54)	71	**<0.001**
Seeing a neurologist	77.8 (91)	117	96.9 (63)	65	**<0.001**
Seeing a physical therapist [b]	40.7 (48)	118	66.7 (42)	63	**0.001**
Power wheelchair	53.8 (64)	119	31.1 (19)	61	**0.005**
Assisted ventilation devices	19.3 (23)	119	8.3 (5)	60	0.08[c]

a Fisher's exact 2-sided test; values in bold are significant at alpha ≤ 0.05
b physical therapist seen outside of school
c Fisher's exact 2-sided test; this variable was significant at p=0.041 for a one-sided Fisher's exact test

5.3 ASSOCIATIONS BETWEEN NIFD VARIABLES

To examine associations between survey variables, correlations were identified and used to generate a regression model. Correlations were observed between increasing child age and decreased independent ambulation, use of wheelchairs and respiratory devices and seeing a cardiologist or pulmonologist. Regression analysis was performed to explore predictors for outcomes of pain and overall life satisfaction.

5.3.1 Regression Analysis

A partial correlation table identified significant associations between selected variables while controlling for survey population. This table was used to reveal overall associations among dataset variables and to identify independent variables to include in linear regression modeling for selected dependent variables. Forward and backward linear regression modeling was generated for child's frequency of bodily pain or discomfort in the past month for the Paper population only (Table 12) and for child's satisfaction with life overall in the past month for the total NIFD population (Table 13) using all significantly associated variables from the partial correlation table. The strongest predictors of bodily pain or discomfort were use of albuterol for strength (beta 0.28) and limitations due to health problems (beta 0.23). The strongest predictors of child's overall life satisfaction were child's satisfaction with friendships (beta 0.53) and child's health other than DMD (beta 0.23).

Table 12: Regression predicting frequency of bodily pain or discomfort in the Paper population*

Model Adjusted R^2 : 0.438		
Variable [a]	**Standardized coefficients Beta**	**Significance**
Use of albuterol for strength	0.281	0.001
Limitations due to health problems	0.229	0.01
Child's satisfaction with school ability	0.196	0.02
Use of manual wheelchair	0.182	0.04
Seeing a cardiologist	0.148	0.07
Use of proton pump inhibitors	0.143	0.08

* Respondents' rating of child's frequency of bodily pain or discomfort in the past month was coded from 0 to 4, starting with "Never" and going to "Every day or almost every day"

a Limitations due to health problems and Child's satisfaction with school ability were coded similarly in that limitations and dissatisfaction increased going from 0 or 1 to higher numbers; Albuterol, manual wheelchair, cardiologist and proton pump inhibitors were all coded with 0 = No and 1 = Yes

Table 13: Regression predicting frequency of child's overall life satisfaction in Internet and Paper populations*

Model Adjusted R^2 : 0.531		
Variable [a]	**Standardized coefficients Beta**	**Significance**
Child's satisfaction with friendships	0.531	<.001
Child's health other than DMD	0.233	<.001
Use of medications for ADD/ADHD	0.179	0.001
Walking independently	-0.154	0.01
Respondent worry for child's behavior	0.119	0.05

* Respondents' rating of child's overall life satisfaction in the past month was coded from 1 to 5, starting with "Very satisfied" and going to "Very dissatisfied".

a Child's satisfaction with friendships used the same coding as overall life satisfaction; Child's health other than DMD and Respondent worry for child's behavior were coded similarly in that health quality worsened and worry increased going from 0 or 1 to higher numbers; ADD/ADHD medications and Walking independently were both coded with 0 = No and 1 = Yes.

Independent variable excluded by the model: Survey population (p = 0.51)

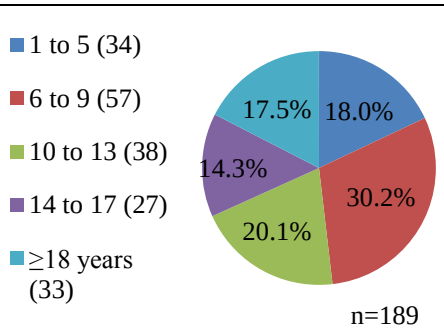
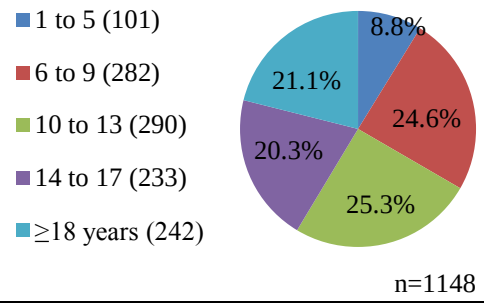
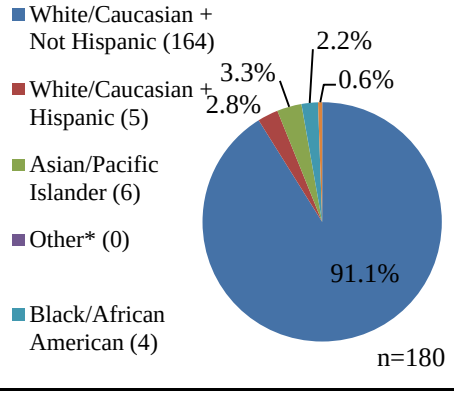
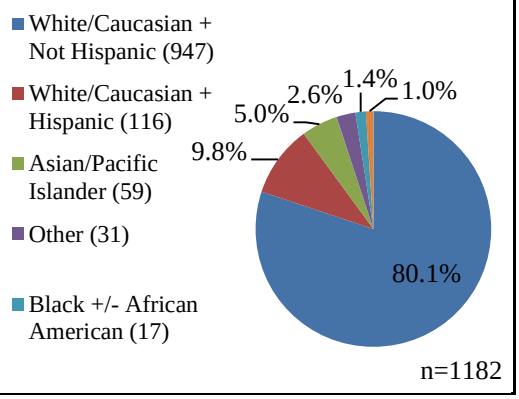
5.4 COMPARISON OF NIFD DATA WITH DUCHENNECONNECT DATA

Age and racial/ethnic background (Table 14) and use of glucocorticoids, walking ability and insurance plans (Table 15) for individuals diagnosed with DMD are compared between NIFD and DuchenneConnect (DC) populations. DuchenneConnect had higher mean ages of and lower percentages of Caucasian/non-Hispanic individuals with DMD. The NIFD population had a larger proportion with traditional insurance plans. More of the DC population was able to walk on their own without help than NIFD. Glucocorticoid use was not significantly different between the populations.

Other diagnoses, problems with medical expense coverage and use of selected services, equipment and devices are also compared in Table 16. The NIFD population reported higher numbers of co-occurring diagnoses; problems with coverage of devices/equipment and medicines; and use of night splints and power wheelchairs. The DC population reported higher

use of therapies (physical, occupational, speech) and manual wheelchairs. Use of breathing devices was not significantly different between populations.

Table 14: Demographics of individuals with DMD between NIFD and DuchenneConnect populations

Variable [p-value]	Population	
	NIFD	**DuchenneConnect**
Age, mean±SD (range) **[p < 0.001[a]]**	11.2 years ±6.1 (1 to 28)	13.1±6.8 (1 to 40) [b]
Age Categories, range in years (n)		
Race/Ethnic background (n) White/Caucasian + Not Hispanic: **[p = 0.0002[c]]**		

SD = standard deviation

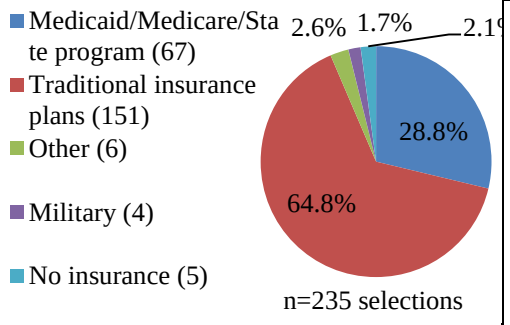
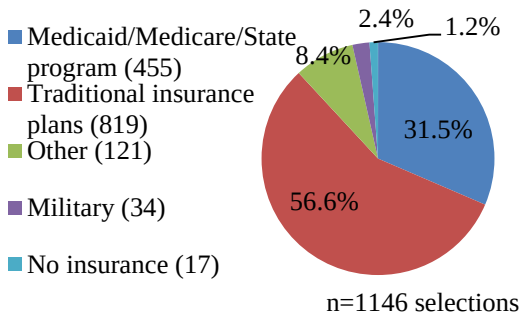
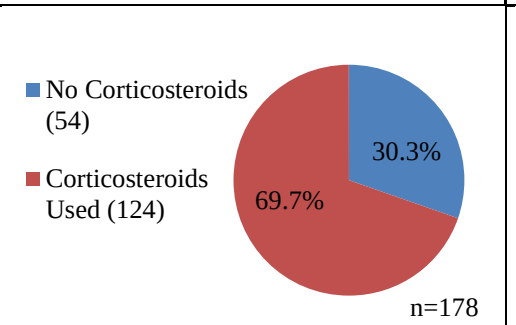
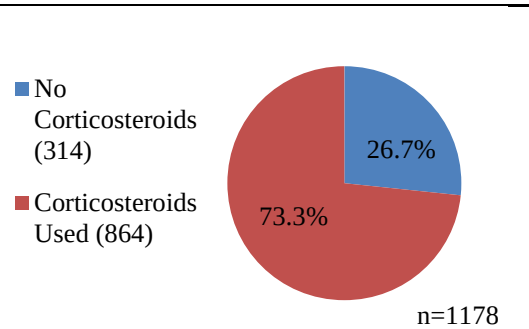
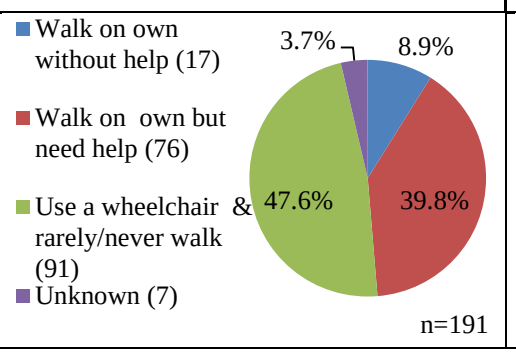
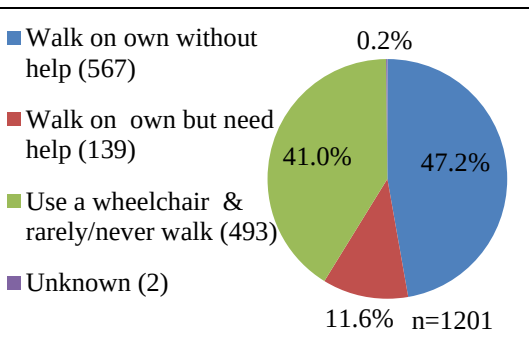
a Independent samples t-test; values in bold are significant at alpha ≤ 0.05 level

b Excludes 23 respondents who said current ages was >40 years. See Methods.

c Fisher's exact 2-sided test by using the shown category to make the data into a dichotomous variable; values in bold are significant at alpha ≤ 0.05 level

* "Other" was an option on the Internet but not Paper version of NIFD

Table 15: Insurance, glucocorticoid use and walking ability between NIFD and DuchenneConnect populations

Variable [p-value]	Population	
	NIFD	**DuchenneConnect**
Insurance plans* (n) Traditional insurance plans: **[0.033 [a]]**		
Gluco-corticoid Use [b] (n) [0.320[a]]		
Walking ability [c] (n) Walk without help: **[<0.001[a]]**		

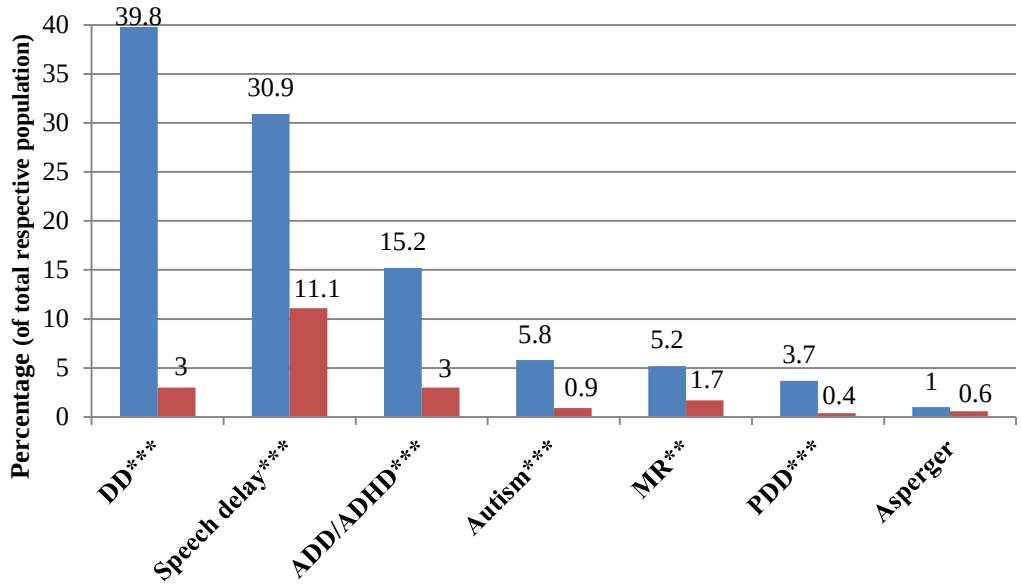
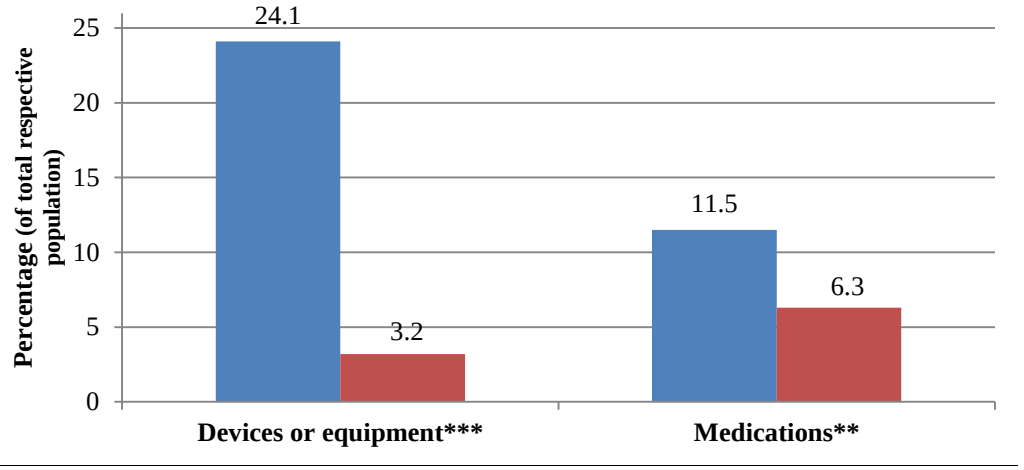
*Insurance: Respondents could select all plans that applied; shown are the percentages of counts out of total pool of selections made by the respondents.

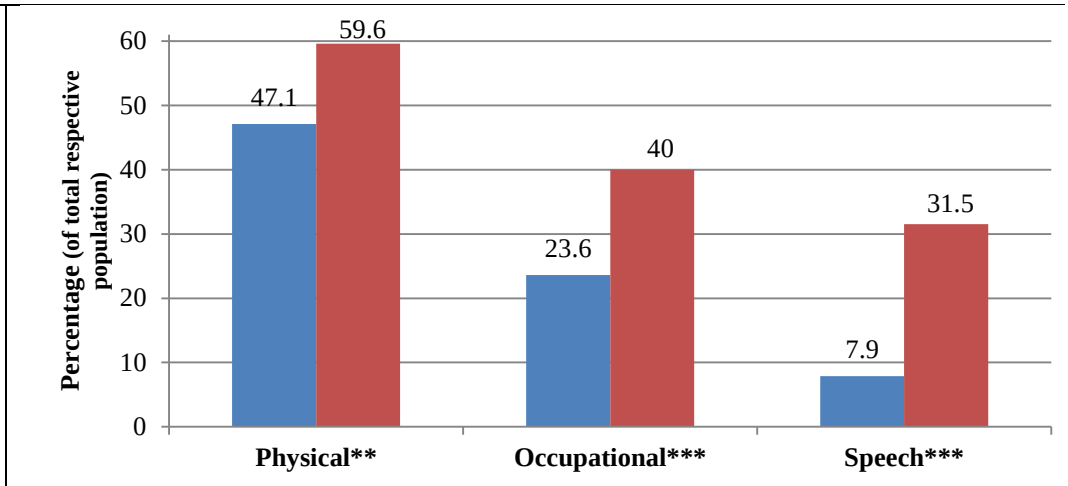
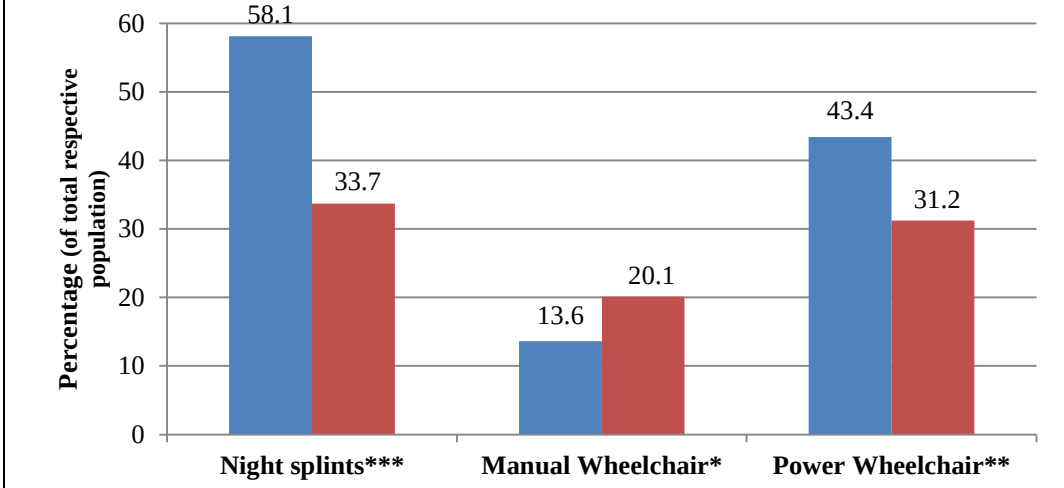
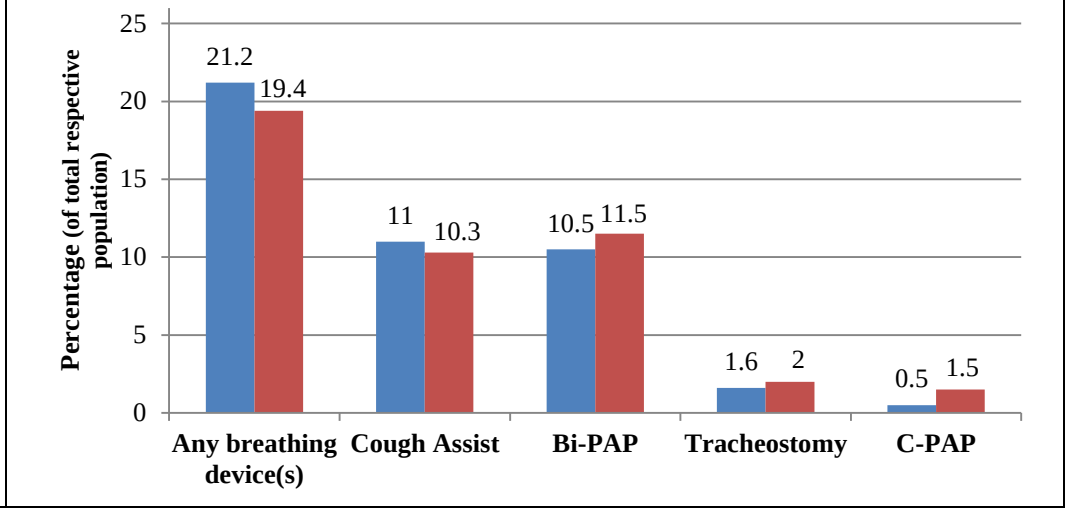
a Fisher's exact 2-sided test by using the shown category to make the data into a dichotomous variable; values in bold are significant at alpha ≤ 0.05 level

b Indicates those who have used glucocorticoids in the past or currently; excluded non-response from NIFD and "Don't know" responses from DC total response counts

c See Methods for data harmonization

Table 16: Comparison of other variables in common between NIFD and DuchenneConnect populations

Variables	Key
	NIFD (N=191) DuchenneConnect (N=1201) * p ≤0.05 ** p ≤0.01 *** p ≤ 0.001
Other Diagnoses	
Problems with coverage for medical expenses	

Therapies	
Use of Night Splints and Wheelchair	
Use of Breathing Devices (no significant differences)	

DD = Developmental delay; ADD/ADHD = Attention deficit; Vision/Hearing = Impairment; MR = Mental retardation; PDD = Pervasive developmental disorder; Bi-PAP = bi-level positive airway pressure; C-PAP = continues positive airway pressure

6.0 DISCUSSION

6.1 CHARACTERIZATION OF THE NIFD DATASET

6.1.1 Demographics

Most respondents (almost 80%) were biological mothers, which may imply their role as primary caregivers among families with DMD. The respondent group included families at all stages of DMD from pre-symptomatic to late non-ambulatory, reflected by the average age of both parents and/or guardians being 42 years ± 8.5 with an age range spanning ages 20 to 66 and the average age of the child being 11.2 years ± 6.1 with an age range spanning ages 1 to 28 years. About 30% of children fell in the 6 to 9 year old group and about 20% in the 10 to 13 year old group. Almost 70% of respondents reported that their child has used glucocorticoids, showing this intervention's role as a standard part of DMD care.

The parents/guardians of the children were well educated with about 59% obtaining at least some college to a graduate or professional degree. This was similar to the education attainment of the US population over 25 years and older (55%) during the NIFD survey period (Census 2012). Most (71%) parents/guardians were working full-time. Of those not working full-time, roughly 13% worked part-time while 16% were not working at all. About half (51%) of

families represented in this study had annual incomes of over $75,000. The median US household income around this time was just over $50,000 (DeNavas-Walt et al. 2012).

6.1.2 Health Status of Child with DMD

As would be expected given the age ranges of children from the survey, a wide range of walking ability was observed. About 57% of children were able to walk independently. Their ability in this regard varied, from being able to walk, run and climb without any difficulty or assistance to walking household distances only with slow progress. About 38% of children could not take any steps and primarily used a power or manual wheelchair.

Pain or body discomfort during the past month was reported at varying frequencies for about 75% of children from the Paper population with almost 33% experiencing it every day or almost every day. This was comparable to 70% of parents who reported bodily pain in their child with DMD in a study by Zebracki et al that included males aged 8 to 18 years with a mean age of 13.9 years (versus NIFD's mean age of 11.2 years) (Zebracki and Drotar 2008). Zebracki et al's study suggested that while pain occurs commonly in DMD, it is likely under-recognized by physicians, who reported less intensity of pain than their patients and patients' parents did, and that regular pain assessment should be implemented in patient care. A study of adult men with DMD found almost 39% reported daily pain and 31% weekly or monthly pain (Rahbek et al. 2005). Pain management was briefly addressed in the DMD care recommendations with recognition of the variation in pain intensity experienced by patients and the need for more research addressing effective interventions throughout the disease course. More attention on palliative care (which addresses pain among other aspects of care) was suggested as an area that should have been discussed more in the DMD care recommendations (Cohn 2010).

The majority of respondents felt their child's health other than DMD was either excellent (31%) or very good (45%), a high rating of health though the question did not query what respondents interpreted as health other than DMD.

Neurocognitive and behavioral conditions have been reported at higher incidences in DMD when compared to the general population. A study of about 350 Dutch and US individuals with DMD found an overall frequency of about 16% for neuropsychiatric disorders in those with DMD (Hendriksen and Vles 2008). In particular, 11.7% had received a diagnosis of ADHD and about 3% of autism spectrum disorder (ASD). These numbers were lower but similar to those found in the NIFD population, which had 15.6% and 6%, respectively, diagnosed with these two conditions. Other smaller studies found a similar prevalence of ASD to NIFD at about 4 to 5% in boys with DMD (Wu et al. 2005; Darke et al. 2006). Hendricksen et al noted that neuropsychiatric disorders can be over or under diagnosed depending on the physician, which could explain some of the variation between study populations (Hendriksen and Vles 2008).

Language delays and verbal deficits have also been noted in boys with DMD (Hinton et al. 2001; Cyrulnik et al. 2007) and were reported to be diagnosed in about 30% of children in the NIFD population. Varying ranges of mental retardation (e.g. 19 to 35%) have been reported in boys with DMD (Cotton et al. 2001; Nereo et al. 2003). Children in the NIFD population were reported to have a lower diagnosis of mental retardation at a little over 5%. Several reports have noted that, despite a mean IQ one standard deviation below the population mean observed in DMD, there is wide variability in intellectual ability in DMD with most having normal intelligence (McDonald et al. 1995; Cotton et al. 2001; Hinton et al. 2001; Poysky 2007).

Though not directly analyzed in the present study, co-occurring ADD/ADHD, ASD, mental retardation and delays likely increase the use of services such as mental health

professionals and of medications for treatment. It is also possible that co-occurrence of other diagnoses has an impact on child's abilities and life quality as was shown in a national survey of children with Fragile X (Bailey et al. 2008). In the present study, use of ADD/ADHD medications was associated with decreases in child's overall life satisfaction.

6.1.3 General Healthcare Coverage, Understanding and Quality

Traditional insurance plans, managed care plans and state-sponsored plans such as Medicaid were the most commonly selected plan types among NIFD respondents. 44% of respondents indicated that at least one major medical expense was not covered by their health insurance plan. Durable medical equipment and therapies (PT, OT, Speech) were the most often selected non-covered expenses at about 38% and 33%, respectively. The latter finding was consistent with respondents who gave concerns about expense or medical insurance as reasons why their child does not see a physical therapist outside of school. This was also consistent with write-in comments from respondents regarding difficulty in obtaining equipment and therapies (Appendix C.3.2).

Almost 61% of respondents felt they understood the inheritance and services needed for DMD very well while 34% felt they understood somewhat well. Respondents' actual understanding of what those services are were not queried and it is likely that parents may have had gaps in knowledge, especially in light of the lack of published DMD care recommendations at the time of survey. Correlation analysis did not reveal any significant associations between respondents' understanding of DMD and demographic, impact and use of service, equipment or medication variables. Parents of children with DMD often serve as advocates for their child, which often requires a good understanding of services and therapies their child needs. This need

for understanding the complexities of care was reflected in some write-in comments from respondents regarding quality of healthcare (Appendix C.3.2). For instance, one respondent wrote, “[We] had to find items of interest relating to DMD and approach the doctor with them”. Another said, “His care is high-quality because I search out the best doctors in the area versed in DMD”.

Over 50% of respondents felt their child had received high quality healthcare since the DMD diagnosis while about 35% felt they had received adequate care. The remainder felt they had either varied or less than adequate healthcare. Lack of coverage for major expenses reported by 44% of respondents is a potential factor in perception of healthcare quality though a significant correlation was not observed between these variables. Issues related to healthcare quality raised in write-in comments about healthcare (Appendix C.3.2) included clinic logistics, doctors’ approaches to care and barriers to needed services/equipment. Correlation analysis did not reveal any significant associations between quality of healthcare since diagnosis and demographic, impact and use of service, equipment or medication variables.

6.1.4 Healthcare Providers

A multidisciplinary approach was suggested as the neurologist and cardiologist represented the providers that the highest percentage of children saw at about 85 and 71% respectively. Roughly half of children saw a pulmonologist or a physical therapist outside of school. In a study of 34 U.S. males with DMD aged 12 to 34 years between 2005-2006, almost 70% had received respiratory care (Arias et al. 2011), which could be higher than NIFD due to an older study population and the term “respiratory care” encompassing more than seeing a pulmonologist. About 61% of NIFD respondents had seen a genetic counselor or geneticist as determined from a

different section of the survey. The higher use of these providers is consistent with their key roles in diagnosis and management of DMD. Further factors related to use of four of these providers are discussed below.

The mean ages at first visit for the top four providers seen (neurologist, cardiologist, pulmonologist, physical therapist) were calculated for the Paper population. The average age for first visit to the neurologist fell within expected ages of diagnosis at an average age of 5 years (SD ± 3). Similarly, age at first visit to a physical therapist 6 years (SD ± 3) was close to typical ages of diagnosis and appropriate initiation of preventive interventions prior to ambulation loss. The mean age at first visit for the cardiologist was 9 years (SD ± 5) reflecting that the 2005 American Academy of Pediatricians (AAP) cardiac recommendation of evaluation at diagnosis (and the DMD care recommendations' guideline at diagnosis or by six years of age at the latest) were not followed by all families (AAP 2005). Similarly, the mean age at first pulmonologist visit was 11 years (SD ± 5) compared to the 2004 American Thoracic Society (ATS) respiratory consensus statement (also adopted by the DMD care recommendations) recommending an early stage visit (ages 4 to 6) and before permanent wheelchair usage for baseline evaluations (Finder et al. 2004). Twice yearly visits are recommended a) after confinement to wheelchair, b) at less than 80% predicted forced vital capacity level and/or c) at age 12 years—thus the children in the NIFD population likely made their first visit around this stage of disease.

Reasons why children did not see the top four providers were explored. For the neurologist, cardiologist and pulmonologist, the largest majority of respondents felt that the child did not need the services of these providers. These respondents represented about 9%, 18% and 29% of the total survey population for each provider, respectively. All (for the neurologist) or roughly three-quarters (for the cardiologist and pulmonologist) of the children these respondents

represented were aged 6 or older, key ages for seeing these providers. Expense and concern about medical insurance were not given as reasons for not seeing these providers by any respondents. Bothwell et al found that pulmonary services and physical therapy were viewed by parents as increasingly important services to be utilized in the future, as their child aged (Bothwell et al. 2002). Thus, it is possible that NIFD respondents, while being aware of the need for these services in the future, did not feel their child needed them at the present time.

About 32% (n=25) of respondents giving a reason why their child does not see a physical therapist also gave the reason of not needing the service (13% of the total survey population). This was the most selected reason for why children did not see a physical therapist. With the exception of one child, these children were all aged 6 years and older. The selection of other reasons why the child did not see a physical therapist was more varied than the other providers, however. Availability, expense and concern for medical insurance were equally given as reasons for not seeing a physical therapist. This agrees with respondents' selection of therapies (including PT) as a top major expense not covered by health insurance plans. Additionally, these responses may reflect a diminished availability of physical therapists specialized in care of children with DMD.

The remaining providers (nutritionist, physiatrist, occupational therapist, social worker, gastroenterologist, mental health therapist and speech therapist) were seen by about a quarter or less of NIFD respondents. Arias et al reported receipt of nutrition counseling and social services in roughly 40% and 35%, respectively, of 34 males with DMD (Arias et al. 2011). Mental health services were received by about 25%. NIFD respondents reported their child saw nutritionists, social workers and mental health therapists less at 27%, 23% and 16%, respectively. Interestingly, over 30% of NIFD respondents reported their child being diagnosed with a speech

delay but only 8.5% reported seeing a speech therapist outside of school. It may be that their child received speech therapy through school.

Additionally, the predominant reason given for why children did not see the other seven providers (nutritionist, physiatrist, occupational therapist, social worker, gastroenterologist, mental health therapist and speech therapist) was also that the respondent felt their child did not need their services (Table C21). It is quite possible these providers were not a part of the child's healthcare team and were therefore deemed to not be needed by the child. Or, an outside referral for such services may have been forgotten or put on low priority by families given the myriad appointments often needed for a child with special needs. Additionally, age likely plays a factor in why respondents feel a service is not needed, as some services may be perceived to be needed at later stages, though the child does not currently use the service. In a small study, Bothwell et al examined families' perceptions of services in DMD (Bothwell et al. 2002). They found that services involving ambulation prolongation were most important, particularly for parents of younger boys. In families with older boys, mental health issues became more important to parents.

Overall, the perception of a child not needing a service may reflect respondents' lack of awareness of the provider's role or importance in their child's care. This emphasizes the need for these specialties to be represented on a child's healthcare team (or at least readily accessible outside of the care team) and for increased awareness of and education on DMD care recommendations. Genetic counselors are poised to serve in an on-going educator role for families as genetic counselors are often present at diagnosis and may serve in care coordination roles. Assisting with distribution of DMD care recommendations, following up with subsequent

family questions and visiting aspects of care that may need to be re-emphasized or initiated are areas where genetic counselors can assist.

6.1.5 Durable Medical Equipment and Devices

Several pieces of equipment and devices are recommended for maintaining mobility and independence as well as respiratory function in DMD. About 60% of respondents reported that their child has used night splints (ankle-foot orthotics), which are indicated for prevention or reducing the progression of contractures through all stages of DMD. Varying percentages of children in each age category reportedly used night splints with the biggest jump in use occurring between the 1 to 5 (24%) and 6 to 9 (72%) age groups, reflecting initiation of this therapy in the older group.

Manual and power wheelchair usage increased with age as would be expected. A large jump occurred between the 6 to 9 and 10 to 13 age groups for both wheelchair types, reflecting the typical ages of ambulation loss. The practice of the initial use of a manual wheelchair followed by use of a power wheelchair was suggested by the higher use of the manual chair in the 6 to 9 and 10 to 13 age group compared to the same or greater use of the power chair in the 14 to 17 and 18 and older age groups. Power wheelchair transition is recommended early when the ability to walk community distances decreases (Bushby et al. 2010b). The NIFD usage of wheelchairs was similar to the Muscular Dystrophy Surveillance Tracking and Research Network's 2007 report of wheelchair usage in males 5 to 24 in four US states (Romitti et al. 2009).

Respiratory devices are a critical aspect of care, particularly in advanced stages of the DMD. Use of lung clearance devices is indicated to prevent collapse and infection of the lungs

(Finder et al. 2004). About 18% of respondents reported that their child used at least one of five devices, including the Emerson Cough Assist device. These children represented 37% of 14 to 17 years olds and about 55% of those 18 years and older. As respiratory function decreases, assisted ventilation becomes increasingly important. About 15% of children have used at least one of six devices representing about a quarter of 14 to 17 years old and about 58% of those 18 years and older. About 81% of the former and 91% of the latter age groups saw a pulmonologist, meaning there were almost 10 to 20% of individuals in these age groups who could benefit from specialty respiratory care. Respondents and their children in this group could have been unaware of changes in respiratory function as declines in lung function can occur silently without the awareness of an individual with DMD. This even further points to the importance of preventive respiratory care. It is also possible these individuals were receiving respiratory monitoring or care through other healthcare providers without seeing a pulmonologist.

6.1.6 DMD's Impact: Worry, Limitations and Satisfaction

The progressive nature of DMD can have a serious impact on a child or adult's physical, emotional and behavioral health. Respondents' were asked to select the amount of worry or concern they had experienced in the past month for these three dimensions of their child's health. Almost all respondents replied to these questions (n=190). When compared side-by-side, the responses showed an increasing amount of worry or concern going from behavioral to emotional to physical health with about 22%, 38% and 44%, respectively, selecting "Quite a bit" or "A lot". These results agree with a study of mothers with a child with DMD which found that behavioral and physical aspects of DMD contributed to maternal stress (Nereo et al. 2003). Parental perception and adjustment to different aspects of health changes throughout the life of their child

with DMD (Abi Daoud et al. 2004; Poysky and Kinnett 2009; Samson et al. 2009) thus levels of worry or concern are also likely to vary by and become intensified at certain stages of disease. Chen et al found that parental health and stress levels were associated with parental perceptions of their child's health status rather than their child's actual health status (Chen and Clark 2010). Respondents in the NIFD study, however, indicated they worried more about emotional, behavioral, and physical domains than they perceived limitations for their children in these areas, though the actual limitation statuses of the children were not determined and could have been lower than reported.

In helping parents with their worries, concerns, and overall adjustment, several recommendations have been made for care providers. Chen et al suggest one way to help parental health and coping is to involve them in their child's care plan and encourage shared decision making. Other recommendations include teaching parents strategies, such as emotion coaching, to help children through emotional problems; use of a care coordinator for each family; eliciting family feedback on satisfaction with care; addressing parental concerns and questions; and maintaining good ties between clinic and advocacy groups (Nereo et al. 2003; Poysky 2007; Poysky and Kinnett 2009)

Respondents' reporting of their child's limitations in schoolwork or activities with friends in the past month somewhat mirrored parental worry or concern in that the reasons why children were somewhat or very limited increased going from behavioral difficulties to emotional difficulties and lastly to problems with health (15.7%, 15.6%, 26%, respectively). In contrast to the respondents' worry or concern, however, the majority of respondents (74 to 84%) felt their children were not limited in these activities by these domains. Thus, reasons other than current limitations in social or school activities contributed to respondents' higher rates of worry/concern

in these domains. These worries could be related to future limitations that respondents foresaw for their child. Additionally, the response rates for the limitations questions were lower, however, with 172 to 173 responses (of a possible 191) so it is possible that more limitations were experienced by children but were not reported.

One study found that 26% of boys with DMD had clinically significant social problems as rated by their parents; age and wheelchair use did not significantly add to the report of behavioral problems (Hinton et al. 2006). Another study of parent-reported psychosocial adjustment in boys with DMD found that while most boys adjusted well, about 17% of boys were at risk for psychosocial problems (Hendriksen et al. 2009). This is similar to the 16% of NIFD respondents who reported some level of limitations due to emotional and/or behavior problems. Because boys with DMD are at increased risk for behavioral problems, both due to the physiological effects of DMD and secondary to disease progression, on-going evaluation is recommended (Polakoff et al. 1998; Poysky 2007; Bushby et al. 2010a). Parents of children with activity limitations were found to be at higher risk for poor physical and mental health, underscoring the impact that DMD can have on the entire family (Witt et al. 2009).

Respondents rated what they perceived their child's overall life satisfaction was during the past month. Of 175 respondents, most felt their child was either very (39%) or somewhat satisfied (42%). Roughly 10% felt their child was somewhat or very dissatisfied. Multiple studies have shown high quality of life or life satisfaction levels in individuals with DMD (Kohler et al. 2005; Rahbek et al. 2005; Baiardini et al. 2011; Simon et al. 2011). Conversely, some self-reported and parent-proxy studies have found some or all health-related quality of life measures assessed to be lower than controls in the DMD population (Grootenhuis et al. 2007; Bray et al. 2010; McDonald et al. 2010). Differences in geography, healthcare systems, survey instrument,

study sample size as well as the subjective nature of satisfaction and quality of life domains are some of the likely factors responsible for such variation. In addition, standard quality of life instruments have been suggested to emphasize clinical aspects of disease and physical functioning (Simon et al. 2011). Though NIFD used proxy measure of child's life satisfaction, the high percentage of respondents who said their child was satisfied agrees with the former set of studies. A thematic study of interviews with nine teenagers with DMD found that most viewed themselves as "as adolescents who just happen to also have chronic disease" and were not in crisis regarding their condition (Pehler and Craft-Rosenberg 2009). These studies emphasize the importance of healthcare providers not making assumptions about a patient's quality of life or life satisfaction, particularly since providers tend to underestimate these aspects in patients (Bray et al. 2010).

Recommendations for care providers to help adjustment in individuals with DMD (and perhaps to thereby increase life satisfaction) include providing patient-centered care and eliciting feedback on that care; assessing and providing support for mental health and educational needs; and promoting independence, educational opportunities and transition to adult care (Rahbek et al. 2005; Poysky and Kinnett 2009; Bushby et al. 2010a)

6.2 DIFFERENCES BETWEEN PAPER AND INTERNET NIFD POPULATIONS

6.2.1 Demographic factors

Significant demographic differences were found between the two populations, the Paper population taking the survey as a baseline evaluation in the CINRG DMD Natural History study

and the Internet population taking the survey from clinic announcement and possibly by finding the survey via Internet search. These differences were found between child and parent/guardian ages, parent/guardian education level and annual family income.

The Internet population had a younger mean child age of 8.8 years (range 1 to 20) versus that of the Paper population's 12.6 years (range 2 to 28). Expectedly, parent/guardian age also followed this trend with the Internet mean parent/guardian age of 40.4 years (range 24 to 58) versus 43.3 years (range 20 to 66).

From a per family perspective, the Internet population had higher education levels when assessed by highest level attained between parent/guardian pairs. About 61% of the Internet population had at least one parent/guardian with a Bachelor's degree or higher versus about 39% of the Paper population. The respective populations did not show significant differences between combinations of employment statuses of parents/guardians but did for annual family income. The Internet population had higher incomes than the Paper population with 80% versus 62%, respectively, having household incomes equal to or higher than $50,000.

Taken together, there are a number of ways these differences could affect the family's experiences. The younger parent age and higher education and income of the Internet population could reflect that this population's familiarity with and better access to online resources. Parents from the Internet population may have been searching the web regarding their son's diagnosis, care or DMD trials and came across the NIFD survey. It is also possible given their child's younger age (and therefore closeness to initial diagnosis) that they were given (or better able to access) newly available resources on recommended care. Families from the Paper population had older children who therefore would be at more advanced stages of DMD. This may have affected

annual income levels (which were lower in the Paper population) as a higher burden of expenses for care occurs as individuals with muscular dystrophy age (Ouyang et al. 2008).

6.2.2 Other Variables

Comparison between populations for key variables revealed five with significant differences: ability to walk independently, seeing a neurologist, seeing a physical therapist, use of power wheelchair and use of assisted ventilation devices. The p-value for assisted ventilation devices approached significance in the Fisher's two-tailed test (p=0.08) and was significant by Fisher's one-tailed test (p=0.04).

Interestingly, the Internet population had a higher proportion of children who saw a neurologist and who saw a physical therapist outside of school when compared to the Paper population. Higher use of these providers could reflect better referrals and/or understanding of these providers' roles in care in the Internet population. The latter is supported by Bothwell et al's finding that families who were closer to the age of diagnosis of DMD (i.e. likely who had younger children with DMD) placed increased importance on neurology, orthopedic services and occupational therapy than families whose child was diagnosed greater than 6 years prior (Bothwell et al. 2002). The difference in seeing a physical therapist could be due to better access to and/or ability to afford such services given that these were reasons given for why children did not see this provider and given the Internet population's higher annual incomes. Lower parent education and income levels, both different between the Paper and Internet populations, were factors found to be associated with being less likely to have a medical home for children with muscular dystrophy (Ouyang et al. 2012). These factors could have affected use of the above providers in the Paper population if they lacked a centralized place to receive care as in the

concept of a medical home. It is curious that the Paper population reported lower use of a neurologist given their involvement in the CINRG DMD Natural History study whose site primary investigators were mostly neurologists. Paper respondents may not have recognized the term “Neurologist” on the questionnaire as the type of doctor at the CINRG site. Again, this points to the importance of families understanding who providers are on the healthcare team and what they do.

The higher use of power wheelchairs and assisted ventilation devices as well as the smaller percentage of individuals walking independently in the Paper population was expected given the significant difference in ages noted between the two populations. Arias et al also noted higher ages between study participants who had received respiratory care versus those who had not (Arias et al. 2011).

6.3 ASSOCIATIONS BETWEEN NIFD VARIABLES

Correlation analysis controlling for survey population was performed across most of the dataset to identify associations between variables. As would be expected, correlations were seen between increasing child age and decreased independent ambulation, use of wheelchairs and respiratory devices and seeing a cardiologist or pulmonologist. Regression analysis was performed to explore predictors for outcomes of pain and overall life satisfaction.

6.3.1 Child's Frequency of Bodily Pain or Discomfort

Regression modeling was performed for the Paper population in regard to the child's frequency of bodily pain or discomfort in the past month. This model accounted for about 44% of the variance in pain frequency in the Paper population. The beta value of all variables was less than or equal to 0.28.

Use of albuterol for strength, experiencing limitations due to health problems, child's increased dissatisfaction with school ability, use of manual wheelchair, seeing a cardiologist and use of proton pump inhibitors were all associated with increases in pain frequency. Among these variables, the strongest predictor (beta of 0.281) was use of albuterol for strength. Use of albuterol, proton pump inhibitors, and seeing a cardiologist suggest respiratory, gastrointestinal and cardiac symptoms that could contribute to discomfort and pain.

Use of manual wheelchair was also a predictor for pain frequency. Use of a wheelchair can introduce multiple discomforts or pain making individualized adjustments, appropriate posturing and physical therapy critical (Bushby et al. 2010b). Wheelchair use also points to increased age and disease progression, which also contribute to experiences of pain.

Not surprisingly, increases in limitations in social and school settings due to health problems and in dissatisfaction with school ability were associated with increases in pain/discomfort frequency. This suggests that pain/discomfort can have consequences for a child's social and academic life. Assessment of functioning in school and community settings can help identify areas where adjustments could improve discomfort or pain levels. Ideally, schools should also work with parents and individuals with DMD to ameliorate these issues (Webb 2005; Bushby et al. 2010a).

Overall, these factors emphasize the importance of regular pain assessment and management throughout a child with DMD's life. Suggested interventions for pain management from the DMD care recommendations include physical therapy, equipment enhancements, pharmacological approaches and, less commonly, surgical procedure (Bushby et al. 2010b).

6.3.2 Overall Life Satisfaction

Regression modeling was performed for the total survey population in regard to the child's overall life satisfaction in the past month. This model accounted for about 53% of the variance in life satisfaction. The beta value of all variables was less than or equal to 0.53.

The strongest predictor for life satisfaction was the child's satisfaction with friendships (beta of 0.531), indicating the importance of social functioning and interactions. Having a chronic health condition can have an isolating effect on social interactions, for the family and particularly for children and teenagers who are forming early life relationships (Samson et al. 2009). A study on psychosocial adjustment in boys with DMD found that while adjustment to the condition for the most part improves over time, relationships with peers were negatively correlated with age (Hendriksen et al. 2009). Pehler et al's interviews with nine teenagers with DMD revealed themes of longing for less dependence on transportation to get to and more physical ability to participate in activities with friends (Pehler and Craft-Rosenberg 2009). In addition, interviewees expressed the desire to be viewed as a person rather than a disabled person by peers. A study of Danish men with DMD found dissatisfaction with interpersonal relationships, particular those of a romantic nature (Rahbek et al. 2005). Taken together, these studies suggest that peer relationships may be an area of difficulty throughout a person's experience with DMD. Almost 8% of NIFD respondents reported that their child was involved

with a support or self-help group (Table C22) and 16% said their child had seen a mental health therapist. Support groups can give increased opportunities for friendships and mental health professionals can give strategies for social interactions. Other suggestions from the DMD care recommendations include peer and school education on DMD; social skills training; modified/adapted sports, camps and youth groups; swim, horse and art therapies; service dogs and internet/chat rooms (Bushby et al. 2010a).

Child's health other than DMD, use of ADD/ADHD medications and respondents' worry for child's behavior were also predictors of life satisfaction, pointing to other conditions and diagnoses as factors influencing respondents' assessment of their child's life satisfaction. This finding highlights the importance of addressing the psychosocial needs of the family and child, particularly in the area of behavioral concerns. Nereo et al found that maternal stress in mothers of boys with DMD was predicted by child's behavioral problems, with higher stress levels in mothers as behavior problems increased in the children (Nereo et al. 2003). Given the potential impact of behavioral problems on the respondent, it is possible that NIFD respondents with higher worry or concern about behavior tended to assess their child's life satisfaction as lower.

Lack of independent walking ability was associated with decreased life satisfaction, which is understandable given the limitations that loss of ambulation can introduce. Impact of decreased abilities was a theme noted in Pehler et al's study as teenagers with DMD expressed desire for the disease to slow down and longed for activities missed due to their physical limitations (Pehler and Craft-Rosenberg 2009). Health-related quality of life studies have also found physical functioning domains to be lower than controls (Bray et al. 2010; McDonald et al. 2010; Baiardini et al. 2011). Interventions to promote mobility and independence are important in transitioning children and adults through decreases in physical abilities. Examples of such

interventions include environmental control systems, transfer devices, customized indoor-outdoor electric wheelchairs and electrically adjustable beds (Eagle et al. 2002; Bushby et al. 2010b).

6.4 COMPARISON BETWEEN NIFD AND DUCHENNECONNECT DATA

Differences between variables examined in NIFD and DC data are discussed below. Overall, the data suggest that the NIFD population represents a more severely affected population (despite having a younger mean age of individuals with DMD) than that of DC. This would be expected at least in part since the NIFD Paper sub-population came from the CINRG DMD Natural History study, which excluded males with DMD who had milder presentation. Additionally, the DC registry came out at time of increased web presence of PPMD and other advocacy groups; it is possible that parents and individuals with DMD became more willing to go online for DMD information and community involvement, especially with availability of more resources. However, the posting of the NIFD web-based survey did have overlap in terms of time with the DC profile. The enhanced marketing resources of PPMD for the DC profile compared to that of the NIFD could explain the significant difference in numbers recruited for the surveys. NIFD was also a substantially longer survey than the DC profile. NIFD Internet participants seemingly represent very motivated individuals who were willing and had the time to complete a lengthy survey.

Taken together, the openness to individuals of any clinical course, wider marketing resources and significantly greater number of participants suggest that DC's data describes a more representative group in terms of natural history and care experiences than that of NIFD.

6.4.1 Demographic and Health Status Factors of Individuals with DMD

The DuchenneConnect population had an older mean age (13.1 years) and wider range of ages at (1 to 40 years) versus NIFD's mean age of 11.2 years (range 1 to 28 years). This difference was not unexpected as the NIFD Paper sub-population represented participants in the CINRG DMD Natural History study which included males with DMD under age 31 and the NIFD Internet sub-population was already shown to have a lower mean age (8.8 years) than the total NIFD mean age.

While both NIFD and DuchenneConnect populations had reduced representation from minority groups (particularly from Black/African American groups), NIFD had less racial and ethnic diversity than DuchenneConnect with about 91% of individuals with DMD being of Caucasian/non-Hispanic background versus 80% in DuchenneConnect. These numbers are higher than census data indicating almost 64% of the U.S. population identifies as Caucasian/non-Hispanic (Humes et al. 2011). The percentage of Black/African Americans in NIFD (2.2%) and DC (1.4%) was much lower than that of 13% in the U.S. population (Humes et al. 2011). This disparity in both populations emphasizes the importance of efforts to promote participation of individuals from minority backgrounds in both study and registry populations to truly depict the experiences of all families with DMD. In 2012, DuchenneConnect initiated a pilot project to address this issue by giving a tablet device to five US neuromuscular clinics so that patients and parents could register and update DC profiles while in clinic (DuchenneConnect 2013).

Glucocorticoid use was not significantly different between NIFD and DC populations, reflecting this treatment's implementation as a standard of care for individuals with DMD. Ambulation ability was found to be significantly different between populations with a higher

number of DC participants able to walk without help or devices. Given the higher mean age of participants in the DC population, it would seem that the DC population should have a higher proportion of non-ambulant or assistance-needing individuals. This finding could be explained, however, by the presence of a wider phenotypic spectrum in DC participants than that of NIFD, whose Paper sub-population was mostly sourced from the CINRG DMD Natural History study that excluded individuals who were ambulant past 13 years without glucocorticoids or ambulant past 16 years with glucocorticoids. It should also be noted that harmonization of walking ability variables between NIFD and DC also required some interpretation on the researcher's part since possible response choices regarding walking ability and setting differed (eleven choices touching on home and outside home walking ability in NIFD versus three choices for outside home walking ability in DC).

With the exception of Asperger syndrome, reported behavioral or cognitive diagnoses made by a doctor or other health professional were significantly lower in the DC population as compared to the NIFD population and the literature. This could reflect more willingness among more severely affected individuals and their families at the time of the NIFD survey to participate both in the CINRG DMD Natural History study and among individuals who chose to take the lengthy NIFD survey online. DC data may be more representative of the incidence of these conditions in the actual DMD population. There were also wording differences between the NIFD and DC profiles that may have influenced respondents' selection. For instance, for the two highest differences in reported diagnoses between the surveys, the DC profile had "global developmental delay" and "speech/expressive language delay (problems explaining & describing things)" versus NIFD's wording of "developmental delay" and "speech delay". It is possible that

a more specific diagnostic term precludes selection of that diagnosis in respondents who are unsure of a diagnosis.

6.4.2 Insurance and Medical Expense Coverage

Respondents for both surveys could select as many types of insurance that applied for the individual with DMD. A higher percentage of traditional insurance plans were selected in the NIFD population versus the DuchenneConnect population, which was found to be a significant difference. Similar percentages of Medicaid and Medicare plans were selected between the two populations. It is possible that more DuchenneConnect participants had traditional insurance plans but chose not to report them as "Prefer not to answer" was an option on this survey.

Significant differences were found for issues with coverage of medical expenses with higher percentages of the NIFD population reporting trouble with device/equipment (24% versus 3%) and medication (11.5% versus 6.3%) expense coverage than the DC population. It is possible that traditional insurance plans, which the NIFD population reported a higher percentage of, are less likely to cover these types of expenses than other plans. A report on disparities in the diagnostic process of DBMD found that those with higher poverty levels had earlier ages of evaluation (Holtzer et al. 2011). One possibility the authors suggest is that these families are more likely to be on Medicaid or other public assistance programs and thus potentially have access to better care than those who are close to the poverty line but do not qualify for Medicaid. These differences in expense coverage between populations could also reflect better coverage over time for medications and equipment shown to be effective for DMD since the NIFD data were older than DC data.

6.4.3 Use of Therapies, Equipment and Devices

Use of physical, occupational and speech therapies were all significantly higher in the DC population. This could be due to a number of reasons. From a survey perspective, NIFD asked about seeing each of these therapists outside of school and in the school setting in a separate survey section (data not analyzed) whereas DC does not distinguish between these two settings. Thus, the DC data could be capturing more use of these services in multiple settings than NIFD. NIFD respondents also reported difficulties getting these therapies covered by health insurance plans, which could contribute to the lower use of such services. Trouble with coverage for therapies was not directly queried on the DC profile. Additionally, better awareness of the importance of such services and possibly better coverage for them could explain higher numbers in the DC population.

Use of night splints and power wheelchairs was significantly higher in the NIFD population and use of manual wheelchairs was significantly higher in the DC population. Usage of night splints was not significantly different between Paper and Internet sub-populations of NIFD. It is possible that, although NIFD respondents were shown to have more issues with coverage of expenses for devices and equipment than DC, they may have had more means to cover these expenses out-of-pocket. The DC profile does not record income data from participants so this could not be directly analyzed. The terminology used on the surveys for this item also differed which could have impacted selection. The NIFD survey referred to them as “night splints” and also provided a definition at the bottom of the page (“braces used to stretch the lower leg muscles at night”). Conversely, the DC profile referred to them as “AFOs (ankle-foot-orthotics)” with no additional definition. DC participants who used these devices may not have selected AFOs if they did not recognize this term.

Higher manual wheelchair use in the DC population and higher power wheelchair use in the NIFD population could also reflect a more severe clinical course in NIFD participants. In addition, ability to cover possible out-of-pocket expenses for power wheelchairs could have influenced the higher usage in the NIFD population, although the NIFD Paper sub-population was shown to have a higher use of power wheelchairs but yet lower incomes than the Internet sub-population.

Interestingly, general use of breathing devices and use of specific devices were similar with no significant differences found between the NIFD and DC populations, despite the older average age in the DC population. This could again support that the NIFD population had a more severe clinical course than the DC population. It should also be noted that there was a larger non-response rate (24%) for the DC question “Are any breathing devices used?” versus NIFD where a collective 6% of respondents did not respond to “Yes/No” questions for specific breathing devices that were combined to harmonize to DC’s breathing devices question. Despite this difference in response to that one item, however, use of specific breathing devices was also similar between the two populations.

6.5 STUDY LIMITATIONS

6.5.1 Survey and Analysis Methods

Using a survey to assess families experience can be a useful tool in gathering a large amount of data with fewer resources. There are several limitations, however, that are introduced by using

this method (Bailey et al. 2010). As a cross-sectional study, NIFD cannot be used to determine cause/effect relationships.

While broader and more specific data can be captured with a detailed survey, NIFD was extremely long (Figure A12). Survey fatigue and lower response rate likely impacted participation. This seemed to be a factor particularly for the Internet population as more surveys were excluded from analysis from this population and, for surveys that were completed, there appeared to be more missing responses than the Paper population. Further, the survey sections examined in this study were located at the end of the Internet version versus at the beginning of the Paper version, thus Internet respondents may have dropped off in participation before they reached these sections. The Paper population may have felt more obligated to complete the NIFD survey since it was a part of their child's participation in the CINRG DMD Natural History study versus the Internet population who likely completed the survey at home and may not have been aware of the survey's length.

NIFD used parent or guardian-reported data, which can introduce more inaccuracy than direct assessment and medical data (Bailey et al. 2010). Respondents who were a part of the CINRG DMD Natural History study, however, did at least have confirmation of DMD diagnosis as a part of inclusion in the study whereas the Internet population did not have such confirmation and could have had an unclear or non-DMD diagnosis. Recall bias is also a limitation, especially for questions asking respondents to remember details on events, interventions used and visits made long ago, especially in older children represented in the survey.

There are limitations to using parent-proxy for perceptual questions about their child such as social functioning and quality of life (Bailey et al. 2010). Moderate to poor agreement between parent and patient reported physical, social and emotional functioning had been

observed in DMD (Bray et al. 2010). Ideally, patient self-reports should be used but sometimes are not possible given the age, health status, or cognitive impairment of a child (Baiardini et al. 2011). Most NIFD questions did not fall into this category but some did, including child's limitations due to emotional or behavioral problems, satisfaction in several domains, and experiences of pain or discomfort.

Some NIFD questions may have been confusing for respondents. For example, the tense of a question may not have captured past use of care. Regarding visits to a provider, the NIFD survey asked "Does your child see" certain providers but did not ask "Has your child ever seen" the providers. This may be the reason why some selected "No" for seeing a provider but then filled in past visit info or why some selected "Yes" for seeing a provider but then gave reason why their child did not see that provider. Missing answers may reflect confusion or no appropriate response for respondent to select.

NIFD did not ask respondents about common surveillance methods (e.g. echocardiograms, forced vital capacity) that may have given a better picture of preventative care children were receiving without seeing a cardiologist or pulmonologist.

DuchenneConnect data were collected from profiles that could be updated. This means that some information could have been outdated for the current age and healthcare usage of registrants if the profile had not been recently updated. DC does not collect demographic data such as income and education so these factors were unable to be compared to the NIFD population. The DC registry requests that users submit genetic confirmation of their diagnosis though not all users have this confirmation nor is it required for participation.

Limiting analysis between NIFD and DC populations to the same age categories (e.g. 1 to 28 years) may have been a better comparison. Another modification that could have been more

insightful to assess changes over time between the two populations would be to use data from separate years (e.g. NIFD 2006-2009 vs. DC 2010 to 2013). Both of these modifications were not possible with data as received from DC but could be pursued with an updated data request to DC.

Data analysis methods used also had some limitations. Multi-collinearity between assigned independent variables was not analyzed in regression modeling however efforts to reduce these effects were made by setting unrelated variables (as determined by a correlation table) as independents.

6.5.2 Study Populations

The NIFD Paper population was a part of the CINRG DMD Natural History study which excluded participants who were walking past the age of 13 (without glucocorticoids) or 16 (with glucocorticoids), were older than age 30 years and were unwilling or unable to participate in the study's protocols and visits. These criteria limit the phenotypic spectrum of the survey population and may select for certain characteristics of people who participate in research. For both Paper and Internet populations, recruiting from clinics and patient organizations can exclude people who are not involved with these institutions and select for participants who are more likely to be accessing multidisciplinary care.

The majority (94%) of children represented in the NIFD survey were White/Caucasian and about 96% were of non-Hispanic origin (Table C17). Roughly 72% of the US population is White and almost 84% is non-Hispanic per 2010 US Census data (Humes et al. 2011). Minority groups were underrepresented in the survey population since DMD affects all races and ethnicities.

Geographical differences in care and in respondent perspectives were not explored in this study. Differences in region have been shown to affect utilization of and costs for care as well as health outcomes of individuals with chronic conditions and muscular dystrophy (Au et al. 2001; Shattuck and Parish 2008; Kenneson et al. 2010). About a third of NIFD respondents were from the Southern region of the United States while about 23 and 28% of respondents were from the West and Midwest, respectively (Table C17). The remainder (almost 15%) was from the Northeast. Thus, some regions, particularly the Northeast, may have been underrepresented among respondents and it is likely that families' region of residence influenced accessibility and availability of services.

6.6 FUTURE STUDIES

There are many questions that remain to be answered related to families' experiences with and utilization of healthcare in DMD. Other factors including surveillance practices (e.g. echocardiogram, forced vital capacity), surgeries and hospital admissions were not examined in this study but make up significant aspects of care for individuals with DMD.

Regional differences in healthcare utilization were not explored in this study but represent another aspect affecting availability and access to multidisciplinary care. Future studies aimed at identifying these differences could point to regions of the US and internationally where adequate care is lacking. Additionally, further study of care received and factors affecting this care in underrepresented groups, including members of minority groups, and in those not seeking care at MDA clinics or other large multidisciplinary sites is warranted. This is especially true in light of studies showing disparities in ages at death and co-morbidities between white and black

males with muscular dystrophies (Kenneson et al. 2010). With national and international efforts by multiple organizations to distribute the DMD care recommendations it will be important to assess families' understanding of what the recommendations entail across geographic and racial lines.

Another area that future studies could address is that of availability of services and implementation of DMD care recommendations from the perspective of health professionals and/or the multidisciplinary clinic. Variations in usage of services and interventions can also stem from different opinions and varying agreement among the healthcare team regarding established care guidelines. One Canadian study of 14 pediatric neuromuscular physicians concluded that multidisciplinary care across the country was consistent with guidelines for DMD care (McMillan et al. 2010). Disparities between perceived availability and use of services between families and healthcare providers had been demonstrated in DMD (Madorsky et al. 1984). In addition, numerous barriers to implementing care guidelines have been discussed from the provider perspective and represent an important area of study regarding the DMD care recommendations (Cabana et al. 1999; Littlejohns and Cluzeau 2000; Larson 2003; Mickan et al. 2011). At the time of the NIFD survey, a Physician survey was distributed to assess the types of services and interventions provided to patients; 93 respondents completed surveys. This data could be a starting point for such a future study. Other similar investigations have been completed or are underway. PPMD's DuchenneConnect site has recently opened a clinic survey for both families and healthcare providers to specify services offered and management practices utilized at clinics. In addition, the previously discussed MDA registry proposal aims to assess service availability and implementation of DMD care recommendations (Scully et al. 2013). In 2012, the CDC posted a grant funding development of a plan to evaluate the delivery of

healthcare in accordance with DMD care recommendations (CDC 2012). These efforts will help identify gaps in care and lend transparency to the level of care provided across care centers, which overall will aid in implementation of the DMD care recommendations.

7.0 CONCLUSIONS

This present study examined healthcare utilization and perceptions from the perspective of families with a child with DMD by describing data from the NIFD questionnaire, which was taken in two formats, Paper and Internet. Analysis of the cross-sectional survey showed that at least half of families were receiving multidisciplinary care and felt that their healthcare was high quality. Mean ages at first visit for the cardiologist and pulmonologist were older than recommended by care guidelines and a minority of respondents whose children did not see key providers felt their child did not need their services. These findings highlight a need for more awareness and education of DMD care recommendations. Use of other sub-specialties was reported by about a quarter or less of respondents. Most children were currently using or had used glucocorticoids, a key treatment in DMD. The majority of the Paper sub-set of the NIFD population reported pain and discomfort in their child in varying frequencies, highlighting an area where individual patient assessment is warranted and broadly where more research and recommendations are needed. Difficulties in covering expenses were noted particularly for durable medical equipment and therapy. Respondents worried most about their child's physical health, followed by emotional well-being and behavior. Most felt their child was not limited in school and social settings by these aspects and that their child was satisfied with life overall.

Significant demographic differences noted between the NIFD sub-populations included higher income and education levels and lower child and parent/guardian ages in the Internet

population. Further, more of the Internet population saw a neurologist or physical therapist. These differences highlight disparities in care that could potentially be explained by socioeconomic differences between families.

Frequency of bodily pain and discomfort was associated with use of medications or providers related to respiratory, GI and cardiac symptoms as well as limitations due to health problems and satisfaction with school ability. Child's satisfaction with life was associated with satisfaction with friendships, indicators of behavioral problems and walking independently. These associations highlight areas where healthcare providers can help families in adjusting and managing aspects of DMD.

Comparison of NIFD data to a more recent dataset from DuchenneConnect, a web-based patient registry, showed a wider phenotypic spectrum in the latter group. DuchenneConnect registrants reported less problems with certain medical expenses and higher use of therapies. These differences point to the need to assess a large population to develop an accurate picture of DMD and hopefully reveal improved awareness and access to important services and interventions.

This study adds to a growing effort by multiple groups to assess the services and interventions used by and experiences of families with DMD. Such study allows for identification of potential barriers to care and areas where families may need more assistance. These are both vital for adequate and consistent implementation of the DMD care recommendations across national and international care centers and for the ultimate goal of improving the lives of individuals and families with DMD.

APPENDIX A

SAMPLE PAGE FROM THE NIFD PAPER SURVEY

Shown on the following page is a sample page from the Medical Care section of the 34-page NIFD Paper survey, demonstrating its lengthy and detailed nature, particular in this section.

M7. Doctors: (Please give us information about the following specialist and tell us how important each is whether or not your child has one.)

Does your child see the following type of doctor?	If no, why not?	If yes, how old was your child at the first visit?	If yes, how often?	How important is this health professional to your child's care (whether your child sees one or not)?
Physiatrist (A rehabilitation doctor) ○ Yes ○ No	○ None available ○ Too expensive ○ Concern about medical insurance ○ Child does not need this service ○ Religious reason ○ Other	☐☐ years ☐☐ months **(for example: 6 years and 9 months)**	○ Only one time ○ Every 3 months ○ Every 6 months ○ Every year ○ As needed	○ Very important ○ Somewhat important ○ Not important
Neurologist *(A doctor who specializes in the nervous system* ○ Yes ○ No	○ None available ○ Too expensive ○ Concern about medical insurance ○ Child does not need this service ○ Religious reason ○ Other	☐☐ years ☐☐ months	○ Only one time ○ Every 3 months ○ Every 6 months ○ Every year ○ As needed	○ Very important ○ Somewhat important ○ Not important
Gastroenterologist (*A doctor who specializes in the digestive system)* ○ Yes ○ No	○ None available ○ Too expensive ○ Concern about medical insurance ○ Child does not need this service ○ Religious reason ○ Other	☐☐ years ☐☐ months	○ Only one time ○ Every 3 months ○ Every 6 months ○ Every year ○ As needed	○ Very important ○ Somewhat important ○ Not important
Cardiologist *(A doctor who specializes in the heart)* ○ Yes ○ No	○ None available ○ Too expensive ○ Concern about medical insurance ○ Child does not need this service ○ Religious reason ○ Other	☐☐ years ☐☐ months	○ Only one time ○ Every 3 months ○ Every 6 months ○ Every year ○ As needed	○ Very important ○ Somewhat important ○ Not important
Pulmonologist *(A doctor who specializes in the lungs and breathing)* ○ Yes ○ No	○ None available ○ Too expensive ○ Concern about medical insurance ○ Child does not need this service ○ Religious reason ○ Other	☐☐ years ☐☐ months	○ Only one time ○ Every 3 months ○ Every 6 months ○ Every year ○ As needed	○ Very important ○ Somewhat important ○ Not important

Figure A13: Sample page from the NIFD Paper survey

APPENDIX B

IRB EXEMPTION LETTER

irb@pitt.edu
PI Notification: IRB determination
March 27, 2012 4:09 PM

University of Pittsburgh
Institutional Review Board

3500 Fifth Avenue
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)
http://www.irb.pitt.edu

Memorandum

To: Rose McGee
From: Christopher Ryan, PhD, Vice Chair
Date: 3/27/2012
IRB#: PRO12030409
Subject: Family Experiences with Duchenne Muscular Dystrophy: Results from a National Survey

The above-referenced project has been reviewed by the Institutional Review Board. Based on the information provided, this project meets all the necessary criteria for an exemption, and is hereby designated as "exempt" under section
45 CFR 46.101(b)(4).
Please note the following information:

- If any modifications are made to this project, use the "**Send Comments to IRB Staff**" process from the project workspace to request a review to ensure it continues to meet the exempt category.
- Upon completion of your project, be sure to finalize the project by submitting a "**Study Completed**" report from the project workspace.

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

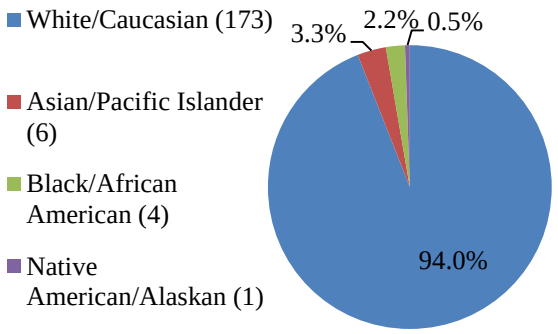
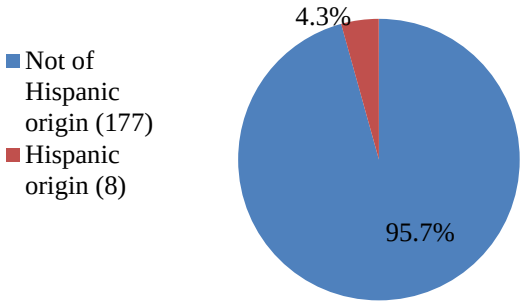
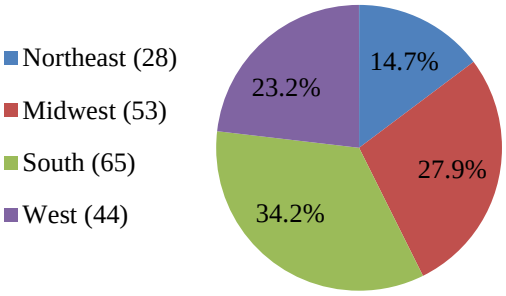
APPENDIX C

DESCRIPTIVE STATISTICS ON NIFD DATA

Data from variables not shown in the Results section but that were summarized in analysis are displayed below.

C.1 DEMOGRAPHIC FACTORS

Table C17: Additional demographic factors

Demographic	Characteristic
Child's Race (n) (total n=184)	
Child's Ethnicity (n) (total n=185)	
Zip Code (n=190) grouped by US Census regions*	

*US Census regions (Census 2013) by state abbreviation:
Northeast: ME, NH, VT, MA, RH, CT, NY, PA, NJ
Midwest: WI, MI, IL, IN, OH, MO, ND, SD, NE, KS, MN, IA
South: DE, MD, DC, VA, WV, NC, SC, GA, FL, KY, TN, MS, AL, OK, TX, AR, LA
West: ID, MT, WY, NV, UT, CO, AZ, NM, AK, WA, OR, CA, HI

C.2 CHILD'S HEALTH STATUS

C.2.1 Other Diagnosis or Condition

Along with the list of prescribed diagnoses (e.g. Autism, Developmental Delay, Asperger's syndrome), respondents could indicate "Yes", "No" or "Don't know" if their child had a diagnosis not listed ("Other") with the ability to specify the diagnosis in a fill-in box. Of 135 respondents to the "Other" category, 20.7% (28) said their child had at least one "Other" diagnosis; two of these said their child had two other diagnoses. The diagnoses specified by respondents were organized by body system and are shown below.

Table C18: "Other" category diagnoses specified by body system

Body System	Diagnoses Specified	% (n) *
Respiratory	asthma; allergies; apnea	18.8 (6)
Cognitive/Behavioral	obsessive compulsive disorder; oppositional defiant disorder; sensory integration disorder; auditory memory deficit; processing delay; Tourette's syndrome	21.9 (7)
Musculoskeletal	Treacher-Collins syndrome; plagiocephaly; scoliosis; bone age delay; hypotonia	15.6 (5)
Cardiovascular	heart defects; heart enlargement; high blood pressure	12.5 (4)
Gastrointestinal/ Genitourinary	acid reflux; constipation; kidney reflux	9.4 (3)
Neurological	epilepsy; seizures	9.4 (3)
Other	hypoglycemia; hypothyroidism; recurrent ear infections; glycerol kinase deficiency	12.5 (4)

* Of n=32 total diagnoses specified by respondents

C.3 MEDICAL CARE

C.3.1 Pediatrician, Distance and Location of Healthcare Providers

Table C19: Details on healthcare providers

Question	Result: % (n)	Total question response
Pediatrician or other child health care provider (outside of the MDA clinic) seen for check-ups every year and for routine health care (Y/N)	Yes: 93.1 (176) No: 6.9 (13)	189
One-way, single trip distance to see health care providers involved in child's health care	Under 10 miles: 14.8 (27) 10 to 50 miles: 52.2 (95) > 50 miles: 33 (60)	182
Location of majority of child's health care providers	MDA clinic: 46.3 (76) Private provider: 31.1 (51) Hospital: 17.1 (28) Other: 4.9 (8) Community free clinic: 0 (0)	164

C.3.2 Write-in Comments on Quality of Child's Healthcare

Forty-four (23% of the total survey population) gave write-in comments about the quality of their child's healthcare since his diagnosis with DMD. Several themes emerged from among respondents' comment including praise for care, dissatisfaction with clinic logistics and/or doctors, and difficulty getting access to certain therapies.

Overall, 15 responses included positive comments on healthcare, using words like "excellent", "great", "high-quality" and "wonderful". One respondent observed improvement of

care since diagnosis, another mentioned the lack of standards of care and a third expressed disappointment with the progress and speed of research.

Comments also addressed issues of logistics in terms of care for the child with DMD. Five respondents noted long distances to care providers and seven mentioned that they switched their care location or moved to access better care. Many of these respondents were traveling across the United States to receive specialized care. Respondents expressed frustration at changes in doctors at clinics, billing practices and difficulties communicating with staff members. Three respondents mentioned dissatisfaction with long wait times for referrals, approvals, equipment and test results.

There were multiple comments on dissatisfaction with doctors. Four respondents cited disagreement on care or opinions between clinic doctors or across aid programs. Several respondents expressed dissatisfaction at the willingness of doctors to try treatments and be proactive in their approach (e.g. “I push for more when the doctors feel they are finished for the time being”). Respondents commented on providers lacking up-to-date information on DMD with one respondent saying that the “quality of healthcare varied widely depending on providers previous experience with DMD and willingness to learn and obtain current information about DMD”.

Some respondents felt that they needed more of certain types of care (e.g. physical therapy, pool therapy, medical equipment) but mentioned barriers to getting them. Six respondents expressed that they had to make demands and/or spend great amounts of time learning about DMD in order to get good care. For example, one respondent said, “The doctor is not forth coming [with] information regarding DMD trials or things going on. We have had to find items of interest relating to DMD and approach the doctor with them”.

C.3.3 Healthcare Providers & Services

Additional variables regarding interactions with healthcare providers are shown in the tables below.

Table C20: Frequency of child's visits to doctors and other health professionals

Doctor	Total response	Only one time % (n)	Every 3 months % (n)	Every 6 months % (n)	Every year % (n)	As needed % (n)
Neurologist	147	6.1 (9)	24.5 (36)	52.4 (77)	8.2 (12)	8.8 (13)
Cardiologist	123	8.9 (11)	2.4 (3)	19.5 (24)	58.5 (72)	10.6 (13)
Pulmonologist	92	5.4 (5)	5.4 (5)	37 (34)	34.8 (32)	17.4 (16)
Physical therapist [a]	88	8 (7)	36.4 (32)	19.3 (17)	15.9(14)	3.4 (3)
Nutritionist	47	23.4 (11)	0 (0)	0 (0)	27.7(13)	19.1(9)
Physiatrist	47	10.6 (5)	27.7 (13)	27.7 (13)	4.3 (2)	29.8 (14)
Occupational [a]	47	6.4 (3)	27.7 (13)	14.9 (7)	14.9 (7)	4.3 (2)
Social worker	38	5.3 (2)	0 (0)	15.8 (6)	23.7 (9)	13.2 (5)
Gastroenterologist	29	27.6 (8)	13.8 (4)	6.9 (2)	13.8 (4)	37.9 (11)
Mental Health	28	3.6 (1)	10.7 (3)	28.6 (8)	7.1 (2)	7.1 (2)
Speech [a]	14	14.3 (2)	50 (7)	7.1 (1)	14.3 (2)	0 (0)

[a] therapist seen outside of school; mo. = month(s); #/week or mo. = number of times per week or month

Table C21: Reasons why child does not see selected providers

Doctor or Health Professional*	Total response	None available % (n)	Too expensive % (n)	Concern about medical insurance % (n)	Child does not need this service % (n)	Other % (n)
Nutritionist	118	7.6 (9)	1.7 (2)	3.4 (4)	72.9 (86)	14.4 (17)
Physiatrist	123	1.6 (2)	2.4 (3)	0.8 (1)	81.3 (100)	13.8 (17)
Occupational [a]	118	8.5 (10)	7.6 (9)	6.8 (8)	55.9 (66)	21.2 (25)
Social worker	122	7.4 (9)	0 (0)	0.8 (1)	85.2 (104)	6.6 (8)
Gastroenterologist	135	3 (4)	0 (0)	0 (0)	89.6 (121)	7.4 (10)
Mental Health	133	3.8 (5)	0.8 (1)	0 (0)	83.5 (111)	12 (16)
Speech [a]	143	2.1 (3)	2.1 (3)	1.4 (2)	83.9 (120)	10.5 (15)

[*] "Religious reason" was an additional answer option but no respondent selected this answer for any provider type

[a] therapist seen outside of school

Table C22: Participation of child and/or respondent in support groups, mental health therapy and clinical trials

Service*	Count (Yes)	Count (No)	Total Response	Percentage (Yes/Total Response)
Support/self help groups[a] (Child)	14	165	179	7.8
Support/self help groups[a] (Respondent)	54	129	183	29.5
Mental Health Therapist (Respondent)	35	144	179	19.6
Clinical trial to treat DMD (Child)	62	119	181	34.3

* Respondents were asked "Does your child/Do you participate in or seek help from the following?" (Yes/No)

[a] to cope with problems related to DMD

Table C23: Frequency of visits to support groups, mental health therapy and clinical trials for child and/or respondent

Service	Total response	Only once % (n)	1-3/week % (n)	1-2/mo. % (n)	Every 6 mo. % (n)	Yearly % (n)	As needed % (n)
Support[a] (Child)	11	18.2 (2)	0 (0)	9.1 (1)	27.3 (3)	9.1 (1)	36.4 (4)
Support[a] (Res)	50	10 (5)	12 (6)	32 (16)	4 (2)	10 (5)	32 (16)
Mental Health[b] (Res)	33	6.1 (2)	27.3 (9)	9.1 (3)	6.1 (2)	3 (1)	48.5(16)
Clinical trial (Child)	53	15.1 (8)	0 (0)	3.8 (2)	34 (18)	11.3 (6)	35.8(19)

[a] support or self help groups to cope with problems related to DMD

[b] mental health therapist

Res= respondent; mo. = month(s); #/week or mo. = number of times per week or month

Table C24: Reasons why child and/or respondent does not participate in support groups, mental health therapy and clinical trials

Service	Total response [a]	None available % (n)	Too expensive % (n)	Concern about medical insurance % (n)	Child/Res does not need this service % (n)	Other % (n)
Support [b] (Child)	150	26.7 (40)	0 (0)	0.7 (1)	40 (60)	32.7 (49)
Support [b] (Res)	118	26.3 (31)	0 (0)	1.7 (2)	31.4 (37)	40.7 (48)
Mental Health[c] (Res)	128	2.3 (3)	4.7 (6)	3.1 (4)	68 (87)	21.9 (28)
Clinical trial (Child)	104	68.3 (71)	0 (0)	0 (0)	11.5 (12)	20.2 (21)

[a] "Religious reason" was an additional answer option but no respondent selected this answer for any service type

[b] support or self help groups to cope with problems related to DMD

[c] mental health therapist

Res = respondent

C.3.4 Medications

Table C25: Medications to help increase or maintain strength: glucocorticoids

Medication	Count (Yes)[a]	Total responses	Percentage	If yes, still use it? [b] % (n)	Total responses
Prednisone	98	175	56	63.6 (63)	99
Prednisolone	13	171	7.6	56.3 (9)	16
Deflazacort	37	172	21.5	80 (32)	40

[a] Response to: "Has your child used the following? (Yes/No)"

[b] Response to: "If yes [child uses medication], does he still use it?"

Table C26: Reasons why glucocorticoids were not used among those who have used them previously

Medication	Total Response [a]	No one prescribed it % (n)	Does not need it % (n)	Too expensive % (n)	Not available % (n)	Too many side effects % (n)	Would not take it % (n)
Prednisone	26	0 (0)	26.9 (7)	0 (0)	0 (0)	73.1 (19)	3.8 (1)
Prednisolone	4	25 (1)	0 (0)	0 (0)	0 (0)	75 (3)	0 (0)
Deflazacort	7	0 (0)	14.3 (1)	28.6 (2)	28.6 (2)	28.6 (2)	0 (0)

[a] Respondents who answered Yes to "Has your child used the following" and selected a reason for why their child was not using glucocorticoids.

Table C27: Medications to help the heart

Medication	Count (Yes)[a]	Total responses	Percentage
ACE inhibitors	22	179	12.3
Beta Blockers	14	177	7.9
Digoxin	11	176	6.3
Diuretics	7	176	4.0
Anti-Arrhythmic	3	172	1.7

[a] Response to: "Has your child used the following? (Yes/No)"

C.3.5 Durable Medical Equipment

Table C28: Use of bracing

Equipment	Count (Yes) [a]	Total Response	Percentage
Short leg braces	46	180	25.6
Long leg braces	18	179	10.1

[a] Response to: "Has your child used the following? (Yes/No)"

Table C29: Reasons why child had not used splints and bracing

Equipment	Total Response [a]	Never suggested % (n)	No need % (n)	He would refuse % (n)	Not available % (n)	Other % (n)
Night splints	65	29.2 (19)	40.0 (26)	20.0 (13)	1.5(1)	9.2 (6)
Short leg braces	121	48.8 (59)	43.0 (52)	5.0 (6)	0 (0)	3.3 (4)
Long leg braces	148	44.6 (66)	48.6 (72)	4.1 (6)	0 (0)	2.7 (4)

[a] "Cannot afford" was an additional answer option but no respondent selected this answer for any equipment type

C.3.6 Pulmonary Devices

Table C30: Use of pulmonary devices

Pulmonary Devices	Count (Yes) [a]	Total responses	Percentage	Current mean age years (SD, range)
Emerson Cough Assist	21	179	11.7	20 (±5;9-28)
Other Lung Clearance Devices [b]	24	180	13.3	17 (±5;4-28)
Tracheotomy	3	179	1.7	23 (±3;21-26)
Other Assisted Ventilation Devices [c]	25	179	14	20 (±4;12-28)
Breathing Exercises	23	176	13.1	16 (±5;3 to 26)

SD: standard deviation

[a] Response to: "Has your child used the following? (Yes/No)"

[b] Respondents selecting one or more of: Vortran percussive nebulizer, Intrapulmonary percussive ventilation (IPV), Chest percussion, TheraVest/Pulmonary Vest

[c] Respondents selecting one of more of: Bi-PAP, C-PAP, Mouthpiece/Sip'n puff

C.3.7 Complementary and/or Alternative Medicine & Supplements

Several questions pertaining to complementary and alternative medicine were asked on the NIFD survey. Of 180 who responded, about 18% (n=32) said they had visited an alternative medicine practitioner to treat their child with DMD. About 42% (n=81) of all respondents selected one or more complementary or alternative medicine approach that their child tried. The 152 selections made among the approach types are shown in Figure C14.

About 49% (n=94) of all survey respondents selected one or more supplement type that their child used. The 276 selections made among the supplement types are shown in Table C31.

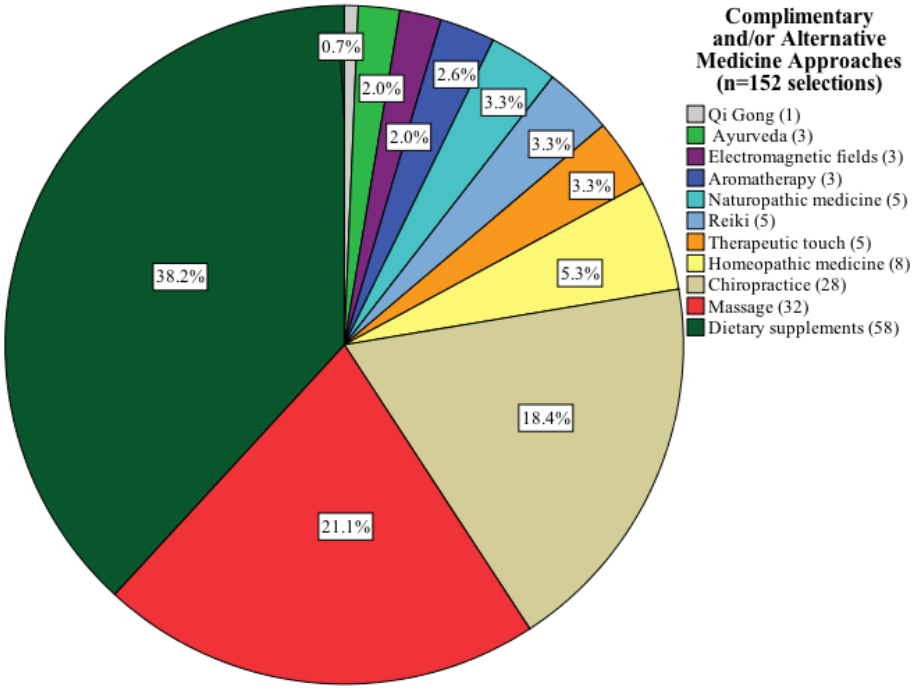


Figure C14: Complementary and/or alternative medicine approaches

Table C31: Use of supplements

Types of Supplements	Responses	
	N	Percent
Calcium	78	28.3%
Coenzyme Q10	45	16.3%
Creatinine	23	8.3%
Vitamin E	22	8.0%
Glutamine	17	6.2%
Magnesium	13	4.7%
Omega-3 Fatty Acids	13	4.7%
Vitamin B12	12	4.3%
Carnitine (L-Carnitine)	10	3.6%
L-Arginine	10	3.6%
Vitamin B6	10	3.6%
Selenium	8	2.9%
Potassium	6	2.2%
Juven	4	1.4%
Omega 6 Fatty Acids	4	1.4%
Cysteine	1	0.4%
Total	276	100.0%

C.3.8 Surgeries

Respondents were able to specify what age and type of surgery or surgeries their child had. 23% (n=44) of respondents reported that their child had one or more surgeries.

Table C32: Surgeries by type and age

Surgery Type	% of total NIFD population (n)	Mean age, years (±SD)	Age range, years
Tendon release (ankle)	14.1 (27)	10.3±2.6	3 to 15
Spinal fusion	13.1 (25)	14.5±1.7	10 to 17
Hip surgery	2.1 (4)	13.75±4.9	9 to 20
Tracheotomy	1.6 (3)	22.7±3.1	20 to 26
Knee	1.0 (2)	12±4.2	9, 15
Other	20 (38)	7.7±7.2	<1 to 20

BIBLIOGRAPHY

AAP (2005). "Cardiovascular health supervision for individuals affected by Duchenne or Becker muscular dystrophy." Pediatrics 116(6): 1569-1573.

Abi Daoud, M. S., J. M. Dooley and K. E. Gordon (2004). "Depression in parents of children with Duchenne muscular dystrophy." Pediatr Neurol 31(1): 16-19.

Anderson, D., S. Dumont, P. Jacobs and L. Azzaria (2007). "The personal costs of caring for a child with a disability: a review of the literature." Public Health Rep 122(1): 3-16.

Appleton, R. E. and P. Nicolaides (1995). "Early diagnosis of Duchenne muscular dystrophy." Lancet 345(8959): 1243-1244.

Arias, R., J. Andrews, S. Pandya, K. Pettit, C. Trout, et al. (2011). "Palliative care services in families of males with Duchenne muscular dystrophy." Muscle Nerve 44(1): 93-101.

Au, D. H., M. B. McDonell, D. C. Martin and S. D. Fihn (2001). "Regional variations in health status." Med Care 39(8): 879-888.

Baiardini, I., C. Minetti, S. Bonifacino, A. Porcu, C. Klersy, et al. (2011). "Quality of life in Duchenne muscular dystrophy: the subjective impact on children and parents." J Child Neurol 26(6): 707-713.

Bailey, D. B., Jr., M. Raspa, M. Olmsted and D. B. Holiday (2008). "Co-occurring conditions associated with FMR1 gene variations: findings from a national parent survey." Am J Med Genet A 146A(16): 2060-2069.

Bailey, D. B., M. Raspa and M. Olmsted (2010). "Using a Parent Survey to Advance Knowledge About the Nature and Consequences of Fragile X Syndrome." American Journal of Intellectual & Developmental Disabilities 115(6): 447-460.

Bakker, J. P., I. J. de Groot, H. Beckerman, B. A. de Jong and G. J. Lankhorst (2000). "The effects of knee-ankle-foot orthoses in the treatment of Duchenne muscular dystrophy: review of the literature." Clin Rehabil 14(4): 343-359.

Balaban, B., D. J. Matthews, G. H. Clayton and T. Carry (2005). "Corticosteroid treatment and functional improvement in Duchenne muscular dystrophy: long-term effect." Am J Phys Med Rehabil 84(11): 843-850.

Baxter, P. (2006). "Treatment of the heart in Duchenne muscular dystrophy." Dev Med Child Neurol 48(3): 163.

Biggar, W. D., L. K. Bachrach, R. C. Henderson, H. Kalkwarf, H. Plotkin, et al. (2005). "Bone health in Duchenne muscular dystrophy: a workshop report from the meeting in Cincinnati, Ohio, July 8, 2004." Neuromuscul Disord 15(1): 80-85.

Biggar, W. D., V. A. Harris, L. Eliasoph and B. Alman (2006). "Long-term benefits of deflazacort treatment for boys with Duchenne muscular dystrophy in their second decade." Neuromuscular disorders : NMD 16(4): 249-255.

Bostrom, K., G. Ahlstrom and H. Sunvisson (2006). "Being the next of kin of an adult person with muscular dystrophy." Clin Nurs Res 15(2): 86-104; discussion 105-106.

Bothwell, J. E., J. M. Dooley, K. E. Gordon, A. MacAuley, P. R. Camfield, et al. (2002). "Duchenne muscular dystrophy--parental perceptions." Clinical pediatrics 41(2): 105-109.

Bourke, J. P. (2006). "Cardiac monitoring and treatment for children and adolescents with neuromuscular disorders." Dev Med Child Neurol 48(3): 164.

Bradley, D. and E. Parsons (1998). "Newborn screening for Duchenne muscular dystrophy." Semin Neonatol 3: 27-34.

Bray, P., A. C. Bundy, M. M. Ryan, K. N. North and A. Everett (2010). "Health-related quality of life in boys with Duchenne muscular dystrophy: agreement between parents and their sons." J Child Neurol 25(10): 1188-1194.

Brooke, M. H., G. M. Fenichel, R. C. Griggs, J. R. Mendell, R. Moxley, et al. (1989). "Duchenne muscular dystrophy: patterns of clinical progression and effects of supportive therapy." Neurology 39(4): 475-481.

Brooke, M. H., G. M. Fenichel, R. C. Griggs, J. R. Mendell, R. Moxley, et al. (1983). "Clinical investigation in Duchenne dystrophy: 2. Determination of the "power" of therapeutic trials based on the natural history." Muscle Nerve 6(2): 91-103.

Brown Jr., R., A. Amato and J. R. Mendell (2008). Muscular Dystrophies and Other Muscle Diseases. Harrison's Principles of Internal Medicine. A. S. Fauci, E. Braunwald, D. L. Kasper et al. New York, McGraw-Hill Medical: 2678-2684.

Bushby, K., R. Finkel, D. J. Birnkrant, L. E. Case, P. R. Clemens, et al. (2010a). "Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management." Lancet Neurol 9(1): 77-93.

Bushby, K., R. Finkel, D. J. Birnkrant, L. E. Case, P. R. Clemens, et al. (2010b). "Diagnosis and management of Duchenne muscular dystrophy, part 2: implementation of multidisciplinary care." Lancet Neurol 9(2): 177-189.

Bushby, K. M., A. Hill and J. G. Steele (1999). "Failure of early diagnosis in symptomatic Duchenne muscular dystrophy." Lancet 353(9152): 557-558.

Cabana, M. D., C. S. Rand, N. R. Powe, A. W. Wu, M. H. Wilson, et al. (1999). "Why don't physicians follow clinical practice guidelines? A framework for improvement." JAMA 282(15): 1458-1465.

CARE-NMD (2013). "About CARE-NMD." http://en.care-nmd.eu/international/about-care-nmd/ Accessed 3/2013.

Case, L. E. (2006). Physical Therapy Management of Dystrophinopathies. Parent Project Muscular Dystrophy Annual Conference. Cincinnati, OH, PPMD.

CDC (2009). "Prevalence of Duchenne/Becker muscular dystrophy among males aged 5-24 years - four states, 2007." MMWR. Morbidity and mortality weekly report 58(40): 1119-1122.

CDC (2012). "Developing a Plan to Evaluate Delivery of Health Care Treatments and Services for Duchenne Muscular Dystrophy (DMD)." http://www07.grants.gov/search/search.do?mode=VIEW&oppId=162033 Funding Opportunity Number CDC-RFA-DD12-1208.

Census (2012). "Percent of Population 25 years and over by Detailed Attainment Level: 2000-2012." US Census Bureau Current Population Survey http://www.census.gov/hhes/socdemo/education/data/cps/historical/fig11.jpg.

Census (2013). Census Regions and Divisions of the United States. Geography Division, U.S. Department of Commerce Economics and Statistics Administration U.S. Census Bureau: http://www.census.gov/geo/www/us_regdiv.pdf.

Chen, A. Y. and P. W. Newacheck (2006). "Insurance coverage and financial burden for families of children with special health care needs." Ambul Pediatr 6(4): 204-209.

Chen, J.-Y. and M.-J. Clark (2010). "Family resources and parental health in families of children with Duchenne muscular dystrophy." The journal of nursing research : JNR 18(4): 239-248.

Chen, J. Y. and M. J. Clark (2007). "Family function in families of children with Duchenne muscular dystrophy." Fam Community Health 30(4): 296-304.

Ciafaloni, E., D. J. Fox, S. Pandya, C. P. Westfield, S. Puzhankara, et al. (2009). "Delayed diagnosis in duchenne muscular dystrophy: data from the Muscular Dystrophy Surveillance, Tracking, and Research Network (MD STARnet)." The Journal of pediatrics 155(3): 380-385.

Cohn, R. D. (2010). "Best practice in Duchenne dystrophy." Neuromuscular disorders : NMD 20(4): 292.

Cotton, S., N. J. Voudouris and K. M. Greenwood (2001). "Intelligence and Duchenne muscular dystrophy: full-scale, verbal, and performance intelligence quotients." Dev Med Child Neurol 43(7): 497-501.

Cripe, L. (2012). Transforming Duchenne Care: Creating a Network of Duchenne Centers of Excellence. Transforming Duchenne Care Meeting, Fort Lauderdale, FL, PPMD.

Cyrulnik, S. E., R. J. Fee, D. C. De Vivo, E. Goldstein and V. J. Hinton (2007). "Delayed developmental language milestones in children with Duchenne's muscular dystrophy." J Pediatr 150(5): 474-478.

Darke, J., K. Bushby, A. Le Couteur and H. McConachie (2006). "Survey of behaviour problems in children with neuromuscular diseases." Eur J Paediatr Neurol 10(3): 129-134.

DeNavas-Walt, C., B. Proctor and J. Smith (2012). "Income, Poverty and Health Insurance Coverage in the United States: 2011." Current Population Reports US Department of Commece Economics and Statistics Administration US Census Bureau: http://www.census.gov/prod/2012pubs/p2060-2243.pdf.

Desguerre, I., C. Christov, M. Mayer, R. Zeller, H. M. Becane, et al. (2009). "Clinical heterogeneity of duchenne muscular dystrophy (DMD): definition of sub-phenotypes and predictive criteria by long-term follow-up." PLoS One 4(2): e4347.

DeSilva, S., D. B. Drachman, D. Mellits and R. W. Kuncl (1987). "Prednisone treatment in Duchenne muscular dystrophy. Long-term benefit." Arch Neurol 44(8): 818-822.

Dooley, J., K. E. Gordon, L. Dodds and J. MacSween (2010). "Duchenne muscular dystrophy: a 30-year population-based incidence study." Clinical pediatrics 49(2): 177-179.

Drachman, D. B., K. V. Toyka and E. Myer (1974). "Prednisone in Duchenne muscular dystrophy." Lancet 2(7894): 1409-1412.

DuchenneConnect (2013). DuchenneConnect 2012 Year-End Report. A. Martin. www.duchenneconnect.org/files/DuchenneConnect_2012_YearEnd_Report.pdf: 5.

Eagle, M., S. V. Baudouin, C. Chandler, D. R. Giddings, R. Bullock, et al. (2002). "Survival in Duchenne muscular dystrophy: improvements in life expectancy since 1967 and the impact of home nocturnal ventilation." Neuromuscul Disord 12(10): 926-929.

Emery, A. E. (1991). "Population frequencies of inherited neuromuscular diseases--a world survey." Neuromuscul Disord 1(1): 19-29.

Engel, A. and B. Banker (1986). Duchenne Dystrophy. Myology: Basic and Clinical. New York, McGraw-Hill. 2.

English, K. M. and J. L. Gibbs (2006). "Cardiac monitoring and treatment for children and adolescents with neuromuscular disorders." Dev Med Child Neurol 48(3): 231-235.

Escolar, D. M., L. P. Hache, P. R. Clemens, A. Cnaan, C. M. McDonald, et al. (2011). "Randomized, blinded trial of weekend vs daily prednisone in Duchenne muscular dystrophy." Neurology 77(5): 444-452.

EUCERD (2011). "Health Indicators for Rare Diseases: Conceptual framework for the use of health indicators for monitoring quality of care." European Union Committee of Experts on Rare Diseases Report September 2011(Accessed at http://www.eucerd.eu/).

Fenichel, G. M., J. M. Florence, A. Pestronk, J. R. Mendell, R. T. Moxley, 3rd, et al. (1991). "Long-term benefit from prednisone therapy in Duchenne muscular dystrophy." Neurology 41(12): 1874-1877.

Finder, J. D., D. Birnkrant, J. Carl, H. J. Farber, D. Gozal, et al. (2004). "Respiratory care of the patient with Duchenne muscular dystrophy: ATS consensus statement." Am J Respir Crit Care Med 170(4): 456-465.

Firth, M., D. Gardner-Medwin, G. Hosking and E. Wilkinson (1983). "Interviews with parents of boys suffering from Duchenne muscular dystrophy." Dev Med Child Neurol 25(4): 466-471.

Gorospe, J. R. and E. P. Hoffman (1992). "Duchenne muscular dystrophy." Curr Opin Rheumatol 4(6): 794-800.

Green, J. M. and F. E. Murton (1996). "Diagnosis of Duchenne muscular dystrophy: parents' experiences and satisfaction." Child Care Health Dev 22(2): 113-128.

Griggs, R. C. (2013). "Study: Finding the Optimum Regimen for Duchenne Muscular Dystrophy (FOR-DMD)." ClinicalTrials.gov. 2013, from http://clinicaltrials.gov/ct2/show/NCT01603407.

Griggs, R. C., R. T. Moxley, 3rd, J. R. Mendell, G. M. Fenichel, M. H. Brooke, et al. (1993). "Duchenne dystrophy: randomized, controlled trial of prednisone (18 months) and azathioprine (12 months)." Neurology 43(3 Pt 1): 520-527.

Grootenhuis, M. A., J. de Boone and A. J. van der Kooi (2007). "Living with muscular dystrophy: health related quality of life consequences for children and adults." Health and quality of life outcomes 5: 31.

Hendriksen, J. G., J. T. Poysky, D. G. Schrans, E. G. Schouten, A. P. Aldenkamp, et al. (2009). "Psychosocial adjustment in males with Duchenne muscular dystrophy: psychometric properties and clinical utility of a parent-report questionnaire." J Pediatr Psychol 34(1): 69-78.

Hendriksen, J. G. and J. S. Vles (2008). "Neuropsychiatric disorders in males with duchenne muscular dystrophy: frequency rate of attention-deficit hyperactivity disorder (ADHD), autism spectrum disorder, and obsessive--compulsive disorder." J Child Neurol 23(5): 477-481.

Henricson, E., R. T. Abresch, A. Cnaan, F. Hu, T. Duong, et al. (2013). "The CINRG Duchenne Natural History Study: Glucocorticoid treatment preserves clinically-meaningful functional milestones and reduces rate of disease progression as measured by manual muscle testing and other commonly-used clinical trial outcome measures." Muscle Nerve *in press*.

Hinton, V. J., D. C. De Vivo, N. E. Nereo, E. Goldstein and Y. Stern (2001). "Selective deficits in verbal working memory associated with a known genetic etiology: the neuropsychological profile of duchenne muscular dystrophy." J Int Neuropsychol Soc 7(1): 45-54.

Hinton, V. J., N. E. Nereo, R. J. Fee and S. E. Cyrulnik (2006). "Social behavior problems in boys with Duchenne muscular dystrophy." J Dev Behav Pediatr 27(6): 470-476.

Holtzer, C., F. J. Meaney, J. Andrews, E. Ciafaloni, D. J. Fox, et al. (2011). "Disparities in the diagnostic process of Duchenne and Becker muscular dystrophy." Genetics in medicine : official journal of the American College of Medical Genetics 13(11): 942-947.

Humes, K. R., N. A. Jones and R. R. Ramirez (2011). "Overview of Race and Hispanic Origin: 2010 Census Briefs." http://www.census.gov/prod/cen2010/briefs/c2010br-02.pdf.

Ireys, H. T., G. F. Anderson, T. J. Shaffer and J. M. Neff (1997). "Expenditures for care of children with chronic illnesses enrolled in the Washington State Medicaid program, fiscal year 1993." Pediatrics 100(2 Pt 1): 197-204.

Jeppesen, J., A. Green, B. F. Steffensen and J. Rahbek (2003). "The Duchenne muscular dystrophy population in Denmark, 1977-2001: prevalence, incidence and survival in relation to the introduction of ventilator use." Neuromuscul Disord 13(10): 804-812.

Kenneson, A. and J. K. Bobo (2010). "The effect of caregiving on women in families with Duchenne/Becker muscular dystrophy." Health Soc Care Community 18(5): 520-528.

Kenneson, A., A. Vatave and R. Finkel (2010). "Widening gap in age at muscular dystrophy-associated death between blacks and whites, 1986-2005." Neurology 75(11): 982-989.

Kinnett, K. (2012). Transforming Duchenne Care Update: Part I - Meeting with the MDA. http://community.parentprojectmd.org/profiles/blogs/transforming-duchenne-care-update-part-i-meeting-with-the-mda, PPMD. 2012.

Koch, S. J., D. E. Arego and B. Bowser (1986). "Outpatient rehabilitation for chronic neuromuscular diseases." Am J Phys Med 65(5): 245-257.

Koenig, M., E. P. Hoffman, C. J. Bertelson, A. P. Monaco, C. Feener, et al. (1987). "Complete cloning of the Duchenne muscular dystrophy (DMD) cDNA and preliminary genomic organization of the DMD gene in normal and affected individuals." Cell 50(3): 509-517.

Kohler, M., C. F. Clarenbach, L. Boni, T. Brack, E. W. Russi, et al. (2005). "Quality of life, physical disability, and respiratory impairment in Duchenne muscular dystrophy." Am J Respir Crit Care Med 172(8): 1032-1036.

Kuhlthau, K., K. S. Hill, R. Yucel and J. M. Perrin (2005). "Financial burden for families of children with special health care needs." Matern Child Health J 9(2): 207-218.

Larson, E. (2003). "Status of practice guidelines in the United States: CDC guidelines as an example." Prev Med 36(5): 519-524.

Littlejohns, P. and F. Cluzeau (2000). "Guidelines for evaluation." Fam Pract 17 Suppl 1: S3-6.

Madorsky, J. G., L. M. Radford and E. M. Neumann (1984). "Psychosocial aspects of death and dying in Duchenne muscular dystrophy." Arch Phys Med Rehabil 65(2): 79-82.

Madsen, A. (2009). The International Heartsongs Project. Quest. http://quest.mda.org/article/international-heartsongs-project, Muscular Dystrophy Association. 16.

Manzur, A. Y., T. Kuntzer, M. Pike and A. Swan (2008). "Glucocorticoid corticosteroids for Duchenne muscular dystrophy." Cochrane Database Syst Rev(1): CD003725.

Manzur, A. Y. and F. Muntoni (2009). "Diagnosis and new treatments in muscular dystrophies." Postgrad Med J 85(1009): 622-630.

Matsumura, K., K. Ohlendieck, V. V. Ionasescu, F. M. Tome, I. Nonaka, et al. (1993). "The role of the dystrophin-glycoprotein complex in the molecular pathogenesis of muscular dystrophies." Neuromuscul Disord 3(5-6): 533-535.

McDonald, C., E. Henricson, R. T. Abresch, J. Han, D. M. Escolar, et al. (2013). "The CINRG Duchenne Natural History Study – A longitudinal natural history study in the era of glucocorticoid therapy: Design of the protocol and methods." Muscle Nerve *In press*.

McDonald, C. M., R. T. Abresch, G. T. Carter, W. M. Fowler, Jr., E. R. Johnson, et al. (1995). "Profiles of neuromuscular diseases. Duchenne muscular dystrophy." Am J Phys Med Rehabil 74(5 Suppl): S70-92.

McDonald, C. M., D. A. McDonald, A. Bagley, S. Sienko Thomas, C. E. Buckon, et al. (2010). "Relationship between clinical outcome measures and parent proxy reports of health-related quality of life in ambulatory children with Duchenne muscular dystrophy." J Child Neurol 25(9): 1130-1144.

McMillan, H. J., C. Campbell, J. K. Mah and C. P. N. Group (2010). "Duchenne muscular dystrophy: Canadian paediatric neuromuscular physicians survey." The Canadian journal of neurological sciences. Le journal canadien des sciences neurologiques 37(2): 195-205.

Mendell, J. R., R. T. Moxley, R. C. Griggs, M. H. Brooke, G. M. Fenichel, et al. (1989). "Randomized, double-blind six-month trial of prednisone in Duchenne's muscular dystrophy." N Engl J Med 320(24): 1592-1597.

Mickan, S., A. Burls and P. Glasziou (2011). "Patterns of 'leakage' in the utilisation of clinical guidelines: a systematic review." Postgrad Med J 87(1032): 670-679.

Miller, A. R., C. J. Condin, W. H. McKellin, N. Shaw, A. F. Klassen, et al. (2009). "Continuity of care for children with complex chronic health conditions: parents' perspectives." BMC health services research 9: 242.

Moxley, R. T., 3rd, S. Ashwal, S. Pandya, A. Connolly, J. Florence, et al. (2005). "Practice parameter: corticosteroid treatment of Duchenne dystrophy: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society." Neurology 64(1): 13-20.

Moxley, R. T., S. Pandya, E. Ciafaloni, D. J. Fox and K. Campbell (2010). "Change in natural history of Duchenne muscular dystrophy with long-term corticosteroid treatment: implications for management." Journal of child neurology 25(9): 1116-1129.

Nereo, N. E., R. J. Fee and V. J. Hinton (2003). "Parental stress in mothers of boys with duchenne muscular dystrophy." J Pediatr Psychol 28(7): 473-484.

Ouyang, L., S. D. Grosse, M. H. Fox and J. Bolen (2012). "A national profile of health care and family impacts of children with muscular dystrophy and special health care needs in the United States." J Child Neurol 27(5): 569-576.

Ouyang, L., S. D. Grosse and A. Kenneson (2008). "Health care utilization and expenditures for children and young adults with muscular dystrophy in a privately insured population." J Child Neurol 23(8): 883-888.

Parsons, E. P., A. J. Clarke and D. M. Bradley (2004). "Developmental progress in Duchenne muscular dystrophy: lessons for earlier detection." Eur J Paediatr Neurol 8(3): 145-153.

Pehler, S. R. and M. Craft-Rosenberg (2009). "Longing: the lived experience of spirituality in adolescents with Duchenne muscular dystrophy." J Pediatr Nurs 24(6): 481-494.

Polakoff, R. J., A. A. Morton, K. D. Koch and C. M. Rios (1998). "The psychosocial and cognitive impact of Duchenne's muscular dystrophy." Semin Pediatr Neurol 5(2): 116-123.

Poysky, J. (2007). "Behavior patterns in Duchenne muscular dystrophy: report on the Parent Project Muscular Dystrophy behavior workshop 8-9 of December 2006, Philadelphia, USA." Neuromuscul Disord 17(11-12): 986-994.

Poysky, J. and K. Kinnett (2009). "Facilitating family adjustment to a diagnosis of Duchenne muscular dystrophy: April 24-25, 2008, Miami, Florida." Neuromuscul Disord 19(10): 733-738.

Rahbek, J., B. Werge, A. Madsen, J. Marquardt, B. F. Steffensen, et al. (2005). "Adult life with Duchenne muscular dystrophy: observations among an emerging and unforeseen patient population." Pediatric rehabilitation 8(1): 17-28.

Rangel, V., A. Martin and H. Peay (2012) DuchenneConnect Registry Report. PLOS Currents Muscular Dystrophy DOI: 10.1371/currents.RRN1309

Rideau, Y., G. Duport, A. Delaubier, C. Guillou, A. Renardel-Irani, et al. (1995). "Early treatment to preserve quality of locomotion for children with Duchenne muscular dystrophy." Semin Neurol 15(1): 9-17.

Romitti, P. A., S. Puzhankara, K. D. Mathews, G. Zamba, C. Cunniff, et al. (2009). "Prevalence of Duchenne/Becker Muscular Dystrophy Among Males Aged 5--24 Years---Four States, 2007." Morbidity and Mortality Weekly Report 58(40): 1119-1122.

Samson, A., E. Tomiak, J. Dimillo, R. Lavigne, S. Miles, et al. (2009). "The lived experience of hope among parents of a child with Duchenne muscular dystrophy: perceiving the human being beyond the illness." Chronic Illn 5(2): 103-114.

Scully, M. A., V. A. Cwik, B. C. Marshall, E. Ciafaloni, J. M. Wolff, et al. (2013). "Can outcomes in Duchenne muscular dystrophy be improved by public reporting of data?" Neurology 80(6): 583-589.

Shattuck, P. T. and S. L. Parish (2008). "Financial burden in families of children with special health care needs: variability among states." Pediatrics 122(1): 13-18.

Simon, V. A., M. B. Resende, M. A. Simon, E. Zanoteli and U. C. Reed (2011). "Duchenne muscular dystrophy: quality of life among 95 patients evaluated using the Life Satisfaction Index for Adolescents." Arq Neuropsiquiatr 69(1): 19-22.

Sussman, M. (2002). "Duchenne muscular dystrophy." J Am Acad Orthop Surg 10(2): 138-151.

TREAT-NMD (2013). "TREAT-NMD global patient registries." http://www.treat-nmd.eu/resources/patient-registries/overview/ Accessed 3/2013.

Vita, G., R. Kirk, H. Lochmuller, K. Bushby and V. Straub (2009). "Early cardiomyopathy in DMD." Neuromuscular disorders : NMD 19: 642.

Webb, C. L. (2005). "Parents' perspectives on coping with Duchenne muscular dystrophy." Child: care, health and development 31(4): 385-396.

Witt, W. P., C. A. Gottlieb, J. Hampton and K. Litzelman (2009). "The impact of childhood activity limitations on parental health, mental health, and workdays lost in the United States." Acad Pediatr 9(4): 263-269.

Wolff, J. (2012). MDA Launches Clinical Neuromuscular Disease Registry. Quest: MDA's Research & Health Magazine. 19: 24-25.

Wu, J. Y., K. C. Kuban, E. Allred, F. Shapiro and B. T. Darras (2005). "Association of Duchenne muscular dystrophy with autism spectrum disorder." J Child Neurol 20(10): 790-795.

Zalaudek, I., R. M. Bonelli, P. Koltringer, F. Reisecker and K. Wagner (1999). "Early diagnosis in Duchenne muscular dystrophy." Lancet 353(9168): 1975.

Zebracki, K. and D. Drotar (2008). "Pain and activity limitations in children with Duchenne or Becker muscular dystrophy." Dev Med Child Neurol 50(7): 546-552.